New! Oral Probiotic Restores Healthy Gums

Live to 100 Years In Good Health

Reduce Dental Plaque by 44%

Vitamin D Reduces Stroke-Induced Brain Damage

PLUS— Overlooked Risk of Proton Pump Inhibitors
Slash After-Meal Insulin/Glucose Spikes
Olive Oil Lowers Breast Cancer Risk by 68%
Two-Per-Day Multi-Nutrient Formula

120 capsules • Item #02014
Compared to commercial formulas like Centrum®, Two-Per-Day has up to 50 times higher potency, plus unique ingredients. Two-Per-Day provides biologically active nutrients such as the 5-MTHF form of folate. Each bottle provides a two-month supply!

Super Omega-3 EPA/DHA with Sesame Lignans/Olive Fruit Extract

120 softgels • Item #01982
A highly refined, super purified Alaskan Pollock fish oil blend plus sesame lignans and potent olive (fruit and leaf) extract provides essential omega-3 fatty acids and vital components of the Mediterranean diet in a smaller-sized softgel that’s easier to swallow.

AMPK Activator

90 vegetarian capsules • Item #01907
Activating AMPK “turns off” many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula promote AMPK activation.

Optimized Resveratrol with Nicotinamide Riboside

30 vegetarian capsules • Item #02031
This trans-resveratrol formula now includes 150 mg of quercetin—2.5 times the previous amount—to support beneficial apoptosis in senescent cells along with nicotinamide riboside that converts to NAD+ to energize cells.

Taurine

90 vegetarian capsules • Item #01827
Research shows taurine can promote new brain cell formation along with whole-body health benefits.

Health Booster (formerly called Super Booster)

60 softgels • Item #01989 (Two-month supply)
Just one daily softgel provides a variety of valuable nutrients including vitamins K1 and K2, blueberry extract, gamma tocopherol, sesame lignans, chlorophyllin, and lycopene, along with vision protecting carotenoids zeaxanthin, meso-zeaxanthin, and lutein.

Advanced Bio-Curcumin® with Ginger and Tumerones

30 softgels • Item #01808
Enhanced-absorbing curcumin with additional inflammation-easing support.

Ultra Natural Prostate

60 softgels • Item #01928
Comprehensive support for the aging prostate gland utilizing standardized nettle root, flower pollen, lignans, plus boron and phospholipids for enhanced absorption.

Triple Action Thyroid

60 vegetarian capsules • Item #02003
Signs of suboptimal thyroid function including “brain fog” and fatigue are often dismissed as “normal aging.” An array of nutrients has been shown to combat many of the complaints that arise from suboptimal thyroid health.

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The SUPER SALE extends to February 1, 2016.

Customers traditionally take advantage of the SUPER SALE to stock up on a year’s supply of their favorite supplements. To place your order, call 1-800-544-4440 or visit www.LifeExtension.com (SUPER SALE pricing available only to customers in the US, Canada, and England.)

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.
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Conventional brushing and flossing may not be enough to ward off deterioration of gums and teeth. Researchers have discovered a targeted probiotic that reduces indicators of plaque buildup, gingivitis, bleeding gums, and pocket depth between gums and tooth roots.
• Personal Consultation with Life Extension
• Blood Testing and Analysis
• The Most Complete Line of Life Extension Supplements

on any dietary, drug, exercise, or other lifestyle change intended to prevent or treat a specific disease or condition should first consult with and seek clearance from a qualified health-care professional.

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The health benefits of eating cold-water fish are robust, yet concerns remain about contaminants found in wild and farm-raised fish.

A fish oil blend derived from pristine waters off the coast of Alaska utilizes a multistep process to remain exceptionally fresh. The result is that this Alaskan-derived fish oil has a greater than 5-fold reduction in the upper level threshold measurement for oxidation.

Current oxidation standards for quality fish oils ensure products that are free from rancidity. This Alaskan-derived fish oil specification advances this premium standard 5-fold better!

High Percentage EPA and DHA
An advantage to higher EPA and DHA fish oil concentrations is smaller-sized omega-3 softgels.

The addition of Alaskan-derived fish oil to the Super Omega-3 supplement group enables the same high-potency EPA/DHA to fit into slightly smaller softgels for easier swallowing.

International Fish Oil Association “Five-Star Rating”
The International Fish Oil Association (IFOS) is an independent organization that tests oils to determine their overall safety and quality. A Five-Star Rating indicates fish oils have been tested to meet very strict standards of quality as determined by EPA and DHA content, and for purity to rule out contamination with heavy metals, radiation, oxidation, and organic pollutants such as PCBs and dioxin.

Alaskan-derived fish oil enjoys the same Five-Star Rating mandated for all fish oils contained in the Super Omega-3 family of supplements.

Benefits of a Mediterranean Diet
The most popular Super Omega-3 formula provides the following potencies in just four smaller softgels:

- Alaskan Wild Fish Oil Concentrate: 4,000 mg
- Providing:
  - Omega-3s: 2,400 mg
    - EPA: 1,400 mg
    - DHA: 1,000 mg
- Polyphen-Oil™ Olive extract (fruit and leaf): 600 mg
- Sesame seed lignan extract: 20 mg

Fish Oil + Olive Fruit Extract = Greater Efficacy
Research findings indicate that a combination of fish oil and olive oil can support a healthy inflammatory response better than fish oil alone. Super Omega-3 incorporates the benefits of both fish oil and olive fruit extract into a single novel formula. A four-softgel serving provides the equivalent polyphenol content of 8 to 12 tablespoons of extra virgin olive oil.

Sesame Lignans Enhance Fish Oil Efficacy
Studies show that when sesame lignans are added to fish oil, there is a greater safeguard against oxidation along with the EPA/DHA fatty acids being directed toward pathways that help with inflammatory reactions.

Comprehensive Protective Benefits
There are hundreds of fish oil supplements on the market. Only one incorporates lifesaving findings to provide omega-3 and olive fruit extracts, along with sesame lignans, in a family of formulas called Super Omega-3.

Super Omega-3
Item #01982 • 120 softgels

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Non-GMO

References

To order Super Omega-3, call 1-800-544-4440 or visit www.LifeExtension.com

Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease.
Gustavo Tovar Baez, MD, operates the Life Extension Clinic in Caracas, Venezuela. He is the first physician in Caracas to specialize in anti-aging medicine.

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

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Örn Adalsteinsson, PhD, is chairman of the Life Extension® Scientific Advisory board. He holds a master’s and doctorate from the Massachusetts Institute of Technology (MIT). He has specialized in human therapeutics including vaccines, monoclonal antibodies, product development, nutraceuticals, formulations, artificial intelligence, hormones, and nutritional supplementation. He has also authored articles and contributed to peer-reviewed publications and served as an editor for the Journal of Medicinal Food.

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John Boik, PhD, is the author of two books on cancer therapy, Cancer and Natural Medicine (1996) and Natural Compounds in Cancer Therapy (2001). He obtained his doctorate at the University of Texas Graduate School of Biomedical Sciences with research at the MD Anderson Cancer Center, focusing on screening models to identify promising new anticancer drugs. He conducted his postdoctoral training at Stanford University Department of Statistics. He is currently president of New Earth BioMed, a nonprofit cancer research corporation that studies mixtures of natural products.

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

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

Xiaoxi Wei, PhD, is a chemist expert in supramolecular assembly and development of synthetic transmembrane nanopores with distinguished selectivity via biomimetic nanoscience. She has expertise in ion channel function and characterization. She founded XTherma Inc., a company developing a radical new highway towards non-toxic, hyper-effective antifreeze agents to fight unwanted ice formation in regenerative medicine and reduce mechanical icing.
Used medicinally for over 4,000 years, curcumin benefits almost every organ in the body. The challenge is that most curcumin supplements are poorly absorbed into the bloodstream and are not well retained in the body. 

Life Extension offers two curcumin supplements that utilize a patented, bio-enhanced preparation that can reach up to 7 times higher concentrations in the blood than standard curcumin. Studies comparing standard curcumin to Super Bio-Curcumin® and Advanced Bio-Curcumin® with Ginger & Turmerones found:

- Nearly 2 times the support for immune health,
- Nearly twice the support for healthy inflammatory response, and
- Approximately double the free-radical fighting support.

Life Extension offers the choice of two super-absorbing curcumin formulas that require only once daily dosing:

- **Super Bio-Curcumin®** provides optimal potency of highly absorbable curcumin.

  OR

- **Advanced Bio-Curcumin® with Ginger & Turmerones** provides the following additional nutrients for those seeking more comprehensive support for prolonged functional inflammatory responses:
  - Ginger to complement curcumin’s health benefits,
  - Turmerones to increase the amount of curcumin inside cells, and
  - Phospholipids to further enhance absorption.

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### Super Bio-Curcumin®

Item #00407 • 60 vegetarian capsules

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### Advanced Bio-Curcumin® with Ginger & Turmerones

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Contains soybeans.

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Bio-Curcumin® and BCM-95® are registered trademarks of Dolcas-Biotech, LLC. U.S. Patent Nos. 7,883,728, 7,736,679 and 7,879,373.

References


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

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.
A startling change occurs around age 65 that decimates our ability to combat infections and malignancies.

This catastrophic event decreases naïve T cells needed to ward off new bacteria, viruses, and cancers. The chart on this page shows how production of these vital immune cells sharply declines as we age.

At the same time naïve T cells are lost, we accumulate senile memory T cells that emit pro-inflammatory signals that wreak havoc in every organ system.¹

One of the most deadly of these inflammatory “signals” is a cytokine called interleukin-6 (IL-6).² Higher IL-6 levels are associated with a 2-fold greater risk of death.³ Higher levels are also involved with multiple degenerative processes including frailty that so many elderly suffer.⁴⁻⁷ A common trait of healthy centenarians is that they have unusually low levels of IL-6.⁸

People associate immune senescence with weakened immune function. It turns out that impaired immunity is only half the problem. Spiraling levels of IL-6 that attack our healthy tissues are another component of immune senescence that must be addressed.⁹

The encouraging news is that significant dollars are being invested to develop technologies to turn back “on” youthful immune function.¹⁰ These immune-restoration therapies will likely add decades to our healthy life spans.

The problem is that many of us can’t wait for bureaucratic delays while our immune systems fall off a cliff. This article will explain what Life Extension® is doing to accelerate restoration of immune competence in aging humans today, including suppressing deadly interleukin-6 levels.
Immune senescence is a leading cause of disability and death in aging humans.11

By way of example, deaths from pneumonia are rare in youth, but spiral upwards as humans mature.12 If you read obituaries (as I do), the number of once-vigorous individuals who perish from opportunistic illnesses caused by immune senescence is startling.

One year ago, Life Extension Magazine® published in-depth reports about underlying causes of immune senescence and what stop-gap measures people should initiate to reverse this deadly trend.13-15

In people over age 65, the top 10 causes of death include influenza, pneumonia, and sepsis.16 **Immune senescence** is a major cause of all these maladies.12,17-22

Cancer, stroke, Alzheimer’s, and heart attack are common diseases of aging.16 These illnesses are all related to immune senescence.

At this time of year, we often hear the term **“immune health”** as people seek to protect against viral infections. The public does not yet understand what causes our immune system to fail as we age.

**More Naïve T Cells Urgently Needed**

Immune imbalance occurs when our aging immune system fails to protect against new cancers/infections, and instead generates inflammatory reactions (including increased IL-6) that attack every cell in our body.

A “naïve” immune cell is one that has not yet been activated.23 Since it is “naïve” (not yet exposed to an antigen), naïve immune cells are primed to effectively respond to new infectious agents and malignancies.

Once exposed, naïve immune cells become memory cells or plasma cells specific to the original antigen. As our internal reservoir of naïve immune cells is decreased, we have less ability to respond to new infections/malignancies.23

A deficit of naïve immune cells combined with overaccumulation of exhausted memory cells decreases the efficacy (antibody response) of vaccinations.24

Exhausted memory T cells are associated with increased risks of coronary heart disease, impaired vascular function, and endothelial dysfunction, along with systemic inflammation.25-30

If we are to guard against the ravages of immune senescence, we need to increase our numbers of naïve cells (“virgin” immune cells), while reducing numbers of senile memory cells.

**Protecting against Immune Senescence Today**

Most Life Extension® customers take nutrients that exert beneficial effects on immune activity.

Zinc and DHEA partially restore thymus function, which is vital to transforming bone marrow-derived immune cells into activated T cells.31-35 DHEA and fish oil help suppress deadly interleukin-6.36-41

A major advance announced last year in combatting immune senescence is an herb called *Cistanche*. This medicinal plant has been used extensively in China to treat the “ailments of aging.”42

Supplementation with *Cistanche* has been shown to increase naïve T cells and natural killer (NK) cells while decreasing memory T cells and pro-inflammatory interleukin-6.43 One of the characteristics of people who live over 100 years is low levels of interleukin-6.8

A prime cause of the severe immune dysfunction suffered by the elderly is a marked decrease in naïve T cells44-46 and functional natural killer cells,47-49 with a concomitant increase in memory T cells.50,51

*Cistanche* counteracts these pathological trends that characterize immune senescence.43
How CistancheBoostsT Cell Productionand Healthy Longevity

*Cistanche* helps restore *progenitors* of peripheral *naïve T cells*, which explains the increase seen in these vital *immune cells* in response to *Cistanche.*

Animals supplemented with *Cistanche* have increased *life spans*, which would be expected by a compound that counteracts *immune senescence.*

*Cistanche* is one of the most popular Chinese herbal medicines and is listed in the Chinese herbal pharmacopeias as having “anti-aging” properties.

One reason Chinese physicians see such impressive therapeutic results is that *Cistanche* restores one of the most prominent bone marrow biomarkers of immune cell formation called *stem cell antigen-1.*

Senile bone marrow loses its ability to produce fresh *naïve immune cells*, which are launched into the bloodstream to differentiate into mature *naïve T* and *natural killer cells*. Bone marrow *stem cell antigen-1* represents the body’s main source of *naïve T cells* in the blood.*Cistanche* appears to have a rejuvenating effect on the bone marrow, something that is generally only available through expensive recombinant drugs.

The beneficial impact of *Cistanche* was demonstrated in an open-label pilot trial of elderly people. This study combined a low-dose of *Cistanche* (*100 mg*) with zinc, vitamin E, vitamin B6, fucoidan, and coenzyme Q10. Not only were markers of *immune senescence* reversed, but the test subjects reported improvements in quality of life, such as not “feeling tired all the time.” This makes sense in light of the multiple adverse effects *immune senescence* inflicts on the body, which includes increased levels of *frailty.*

There are other factors that weaken immune function in the elderly that *Cistanche* has been shown to counteract. These will be described in depth in the article beginning on page 34 of this month’s issue.

*Cistanche* represents an important advance in our ability to restore vital components of our aging immune systems. Its low cost makes it readily affordable.

SuppressingDeadly Impact of IL-6

One way of describing “aging” is that beneficial factors (such as *naïve T cell* production) *decrease* while detrimental ones (like *interleukin-6*) *increase*.

*IL-6* levels are especially high in patients with autoimmune conditions where an out-of-control immune system attacks one’s own tissues. High serum *IL-6*, as seen in *rheumatoid arthritis*, for instance, is regarded as a reliable biomarker of high-grade *inflammation*.

When it comes to “normal” aging, elevated *IL-6* contributes to the chronic destruction of our bone, heart valves, neurons, and other tissues, while the DNA damage it inflicts accelerates aging processes and malignant transformation of healthy cells.
Life Extension® has published a number of articles over the past several decades about the critical need for aging humans to suppress chronic inflammatory inducers like interleukin-6.

I am pleased to announce that a potent new weapon to reduce IL-6 has been added to an immune-restoration formula that many of our customers take daily. The cost of this novel tea extract is so low that the price of this blend of beneficial immune nutrients remains the same as last year.

When this tea extract was given by itself to a group of 90 patients (30-65 years) with metabolic syndrome, the following reductions in inflammatory markers were observed:67

- C-reactive protein (CRP) was reduced by 26%
- Tumor necrosis factor (TNF-α) was reduced by 23%
- Interleukin-6 (IL-6) was reduced by 21%

In addition to suppressing IL-6 and other inflammatory factors, this tea extract was shown to favorably alter genes (such as mutant p53) involved in tumor cell growth.68

Making Major Strides...

We are rapidly entering a new paradigm in counteracting age-related disease.

Scientific studies document how certain nutrients that Life Extension® supporters have taken for decades (like DHEA and zinc) help protect against immune decline, while guarding against chronic inflammatory factors.70-75

Consumers now have access to an arsenal of novel compounds to counteract the underlying factors that characterize immune senescence.

An impressive array of clinical research is being investigated to induce systemic age reversal in elderly humans by utilizing bone marrow-mobilized factors from young blood donors.76

Your purchases of these nutrient formulas from Life Extension® help to fund avant-garde research at prestigious medical facilities aimed at gaining control over pathological aging processes.

Obtain Latest Formulas at Year’s Lowest Prices

This is the time of year when we discount prices on every one of our advanced nutritional formulas. Longtime supporters know to take advantage of this once-a-year Super Sale to stock up on their favorite supplement formulas.

What should comfort supporters more than anything else are the three novel methods to counteract aging we have introduced over the past 12 months.

One involves activating a cellular enzyme (AMPK) that declines with aging and is responsible for myriad of age-related disorders.

The second (introduced three weeks ago) suppresses an enzyme (MAO-B) that accelerates brain aging and causes maturing people to lose their sense of well-being.

The third is an enhancement to an immune-protection formula that suppresses deadly inflammatory factors such as IL-6, TNF-α, and C-reactive protein.

Our Commitment to Your Health

No organization is more dedicated to combatting disease, senescence, and premature mortality than Life Extension®. Your support via supplement purchases enables us to contribute to scientists involved in unprecedented biomedical research endeavors.

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

For longer life,

William Faloon
Inflammatory Markers Predict Human Mortality

A study of community-dwelling people over age 80 was done to investigate whether interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α) levels predict all-cause mortality.

Baseline levels of these inflammatory markers were taken and the subjects followed up for a period of four years.

After adjusting for potential confounders, those with high levels of IL-6 were **2.18 times more** likely to die, while study subjects with high CRP were **2.58 times more** likely to die.

While TNF-α by itself did not increase mortality rates, those with all three inflammatory markers above the median had the **highest mortality risk** during the four-year study period. The doctors who conducted this study concluded:

> Low levels of inflammatory markers are associated with better survival in elderly, independently of age and other clinical and functional variables.⁷⁶⁹

References

28. Olson NC, Doyle MF, Jenny NS, et al. Decreased naive and increased memory CD4(+) T cells are associated with subclinical atherosclerosis: the multi-ethnic clinical atherosclerosis: the multi-ethnic


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DHEA is a critically important hormone, but its production declines sharply as we age. By the time you reach 70, your DHEA levels are likely to be 75-80% lower than when you were at your peak.1-4

Scientists are discovering numerous health benefits when aging people restore their DHEA to youthful ranges. DHEA therapy has been shown to:

• Support healthy arterial structure and function5,6
• Support endothelial health by helping with blood flow7
• Promote insulin sensitivity8,9
• Benefit the normal aging brain10,12
• Improve mood and alleviate melancholy13
• Protect hip bone and spine bone mineral density14
• Enhance the increases in muscle mass and strength in the elderly with resistance exercise15
• Boost a broad array of immune system cells and signaling molecules16

By supplementing with DHEA, you can get your levels back to youthful values. An ideal daily dose of DHEA for many healthy aging people is 25 mg. Life Extension’s® convenient, economical 25 mg capsules are a popular way to consume the precise amount of DHEA your body may need.

DHEA 25 mg
Item #00335 • 100 capsules

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Each bottle lasts a typical user over three months!

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

CAUTION: Do not use DHEA if you are at risk for or have been diagnosed as having any type of hormonal cancer, such as prostate or breast cancer.
Non-GMO

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.
Aspirin Use Associated with Improved Gastrointestinal Cancer Survival

The 2015 European Cancer Congress was the site of a presentation on the finding of longer overall survival associated with use of aspirin following diagnosis of gastrointestinal cancer.*

Martine Frouws, MD, analyzed data from 13,715 men and women diagnosed with a GI cancer from 1998 to 2011. Aspirin was used prior to cancer diagnosis by 30.5% of the subjects and by 8.3% after being diagnosed.

Nearly 28% of the patients were still alive for at least five years over a median follow-up period of 48.6 months. Among those who used aspirin after diagnosis, the chance of surviving was double that of nonusers.

According to European Society for Medical Oncology spokesperson Nadir Arber, MD: “Aspirin may serve as the magic bullet because it can target and prevent ischemic heart disease, cancer, and Alzheimer’s disease, the three major health catastrophes in the third millennium.”

Editor’s Note: “Medical research is focusing more and more on personalized medicine, but many personalized treatments are expensive and only useful in small populations,” Dr. Frouws observed. “We believe that our research shows quite the opposite. It demonstrates the considerable benefit of a cheap, well-established, and easily obtainable drug in a larger group of patients, while still targeting the treatment to a specific individual.”

* European Cancer Congress. 2015 Sep 25-29.

Junk-Food Diet May Shrink the Brain

An article in BMC Medicine reports that older individuals who eat an unhealthy Western diet have smaller brains, which researchers say is further proof that junk food has a terrible impact on health.*

The results of the study, conducted by researchers at Deakin University and the Australian National University, suggest that older adults who consume more junk foods, such as sweet drinks, salty snacks, and processed meats, have smaller left hippocampi. It also shows that older adults who eat healthier foods, such as vegetables, fruits, and fish, have larger left hippocampi. These relationships existed over and above other factors that may explain these associations, such as gender, levels of physical activity, smoking, education, or depression.

The researchers used magnetic resonance imaging to measure the size of hippocampus in Australian adults aged 60-64 years. They also measured the participants’ regular diets and took into account a range of other factors that could affect the hippocampus. These findings that consuming junk foods accelerates brain atrophy have substantial relevance for both dementia prevention and mental health.

Editor’s Note: “This study sheds light on at least one of the pathways by which eating an unhealthy diet may influence the risk for dementia, cognitive decline, and mental disorders such as depression and anxiety in older people,” said lead author Felice Jacka. “However, it also points to the importance of diet for brain health in other age groups. As the hippocampus is critical to learning and memory throughout life, as well as being a key part of the brain involved in mental health, this study underscores the importance of good nutrition for children, adolescents, and adults of all ages.”

Chronic Diseases May Increase Risk of Dementia

In a new study of older adults published in the Journal of the American Geriatric Society, having multiple chronic conditions was linked with an increased risk of mild cognitive impairment (MCI) or dementia.*

Researchers assessed 2,176 cognitively normal participants with an average age of 78.5 years who were followed for a median of four years. Participants with more than one chronic condition were 38% more likely to develop MCI/dementia. Participants with four or more conditions had a 61% increased risk compared with those with one or no condition. Men also had a higher risk than women.

“We were not able to investigate the specific mechanisms by which multimorbidity contributes to cognitive impairment; however our findings are consistent with the hypothesis that multiple etiologies may contribute to late-life cognitive decline and thus emphasize the importance of prevention,” said study author Dr. Rosebud Roberts. “They also emphasize that chronic diseases, once diagnosed, should be efficiently managed.”

While the researchers are confident about the link between chronic illness and cognitive impairment, they note they are uncertain about why it occurs, but offer different theories. “An important potential mechanism is through cardiovascular diseases: hypertension, hyperlipidemia, and cardiac diseases, specifically CAD,” the authors wrote. They add that chronic conditions such as arthritis limit mobility and physical activity, leaving people more susceptible to cardiovascular disease, which in turn may increase cognitive impairment. Aging people with concurring chronic conditions are also more likely to have harmful interactions with an increasing number of medications, which may leave them vulnerable to dementia.

Editor’s Note: The findings suggest that the prevention of chronic diseases may help aging adults maintain their mental health.


Omega-3 Fatty Acid Levels Predict Decreased Arterial Stiffness

In an article published in the Journal of Nutrition, Ilse Reinders and colleagues report an association between higher plasma phospholipid omega-3 polyunsaturated fatty acids (PUFAs) and lower pulse wave velocity, a measure of arterial stiffness which, when increased, has been correlated with a greater risk of cardiovascular disease and related mortality.*

The study involved participants in the ongoing Age, Gene/Environment Susceptibility–Reykjavik (AGES-Reykjavik) Study. Of those who had plasma phospholipid polyunsaturated fatty acids measured upon enrollment, 501 subjects had carotid-femoral pulse wave velocity measured at a five-year follow-up examination.

Higher total plasma omega-3 polyunsaturated fatty acids and individual omega-3 fatty acids EPA and DHA were associated with lower pulse wave velocity. In contrast, subjects whose total plasma omega-6 fatty acids and the omega-6 fatty acid linoleic acid were higher had increased carotid-femoral pulse wave velocity measurements.

Editor’s Note: “Our results for plasma phospholipid omega-3 PUFAs are confirmed by a recent randomized, controlled trial showing that omega-3 supplementation resulted in lower carotid-femoral pulse wave velocity,” the authors remark. “The effect of omega-3 PUFAs on carotid-femoral pulse wave velocity might be explained by improved endothelial function and a decrease in inflammatory markers.”

Inflammation Drives Colorectal Cancer Metastasis

An article published in Gastroenterology reports the results of research that uncovered an effect for the inflammatory mediator prostaglandin E2 (PGE2) as a driving force in the metastasis of colorectal cancer.*

“The normal role of PGE2 is to come to the rescue when you do something like cut your finger,” explained lead researcher Raymond N. DuBois, MD, PhD. “It attracts the body’s immune cells and stimulates pathways that heal the wound site. The level of PGE2 goes up and then goes down within a few days of healing the wound. But in cancer, the cells keep making PGE2 chronically, so it’s like this wounding process that never heals. In doing so, it generates these cancer stem cells that promote cancer progression and metastatic spread.”

By measuring levels of prostaglandin E2 in colorectal carcinoma specimens and normal tissues, Dr. DuBois and associates found a correlation between the compound and colon cancer stem cell markers.

Editor’s Note: “We’ve long known that simple things like taking aspirin or other anti-inflammatory drugs (called nonsteroidal anti-inflammatory drugs, or NSAIDs), have beneficial effects on reducing the risk of colorectal cancer,” Dr. DuBois observed. “But non-aspirin NSAIDs can cause serious cardiovascular side effects when taken over a long period of time, so we’ve needed to discover better drug targets. This study points us in the right direction.”


Low Vitamin D Levels Linked to Memory Loss

A study published in JAMA Neurology found that older adults with low vitamin D levels may lose their memories and thinking abilities faster than those with normal levels, especially when it comes to memory loss related to Alzheimer’s disease and dementia.*

Dr. Joshua W. Miller and colleagues at University of California, Davis, Alzheimer’s Disease Center, looked at the association between blood levels of vitamin D and changes in memory and thinking ability in 318 adults over an average of five years.

The researchers defined adequate blood levels of 25-hydroxyvitamin D—the form of vitamin D generated when the body converts the vitamin D made in the skin by sunlight and consumed from foods like eggs, oily fish, and milk—to be in the range of 20 ng/mL to 50 ng/mL. Insufficient levels are 12 ng/mL to less than 20 ng/mL, and levels below 12 ng/mL are deficient.

Study participants had a mean age of 76 and were cognitively normal, had mild cognitive impairment, or dementia. Researchers found that more than 60% had low vitamin D levels, including more than a quarter who had a deficiency. Individuals with dementia had lower vitamin D levels (about 16.2 ng/mL) than those with mild cognitive impairment (average 20 ng/mL) or whose memory was normal (19.7 ng/mL). Over the course of the study, those with low vitamin D levels showed an accelerated decline in executive function—working memory, reasoning, task flexibility, problem solving, planning, and execution—and in the ability to remember their own past personal experiences. These rates of decline were similar for individuals who had normal brain function at the beginning of the study and for those who already had dementia or mild cognitive impairment.

Editor’s Note: Among people with cognitive impairment, an estimated 70% to 90% have insufficient vitamin D. “This work, and that of others, suggests that there is enough evidence to recommend that people in their 60s and older discuss taking a daily vitamin D supplement with their physicians,” Miller said.

* JAMA Neurology. 2015 Sep 14.

Resveratrol Benefits Those with Alzheimer’s

The results of a trial reported in Neurology reveal an association between supplementation with resveratrol and improvement in markers of Alzheimer’s disease.*

One hundred-nineteen men and women diagnosed with probable Alzheimer’s disease were randomized to receive a placebo or 500 mg synthetic resveratrol daily, with a dose increase of 500 mg every 13 weeks that ended with a 1,000 mg dose twice per day at the end of the 52-week study. Plasma and cerebral spinal fluid were analyzed for resveratrol and its metabolites, and amyloid beta 40 and 42 at the beginning and end of the study.

While plasma and cerebrospinal amyloid beta 40 levels had significantly decreased among the placebo group by the end of the study, they remained relatively stable among those who received resveratrol. “A decrease in amyloid beta 40 is seen as dementia worsens and Alzheimer’s disease progresses,” explained lead author R. Scott Turner, MD, PhD.

Editor’s Note: “It does appear that resveratrol was able to penetrate the blood brain barrier, which is an important observation,” Dr. Turner noted. “Resveratrol was measured in both blood and cerebrospinal fluid.”

* Neurology. 2015 Sep 11.
Olive Oil Reduces Breast Cancer Among Women at Risk of Cardiovascular Disease

A trial reported in JAMA Internal Medicine found a significantly lower risk of invasive breast cancer among women who consumed a Mediterranean diet supplemented with extra virgin olive oil in comparison with women assigned to a control diet who were given advice to eat a reduced fat control diet.*

The trial included 4,282 women enrolled in the PREDIMED study who were at increased cardiovascular disease risk due to the presence of diabetes or other factors. Subjects were assigned to a Mediterranean diet supplemented with olive oil or nuts, or a control diet.

After a median follow-up of 4.8 years, 35 cases of invasive breast cancer were identified. While both Mediterranean diets were associated with a reduced risk of the disease, the diet supplemented with olive oil was associated with the lowest risk, which was 68% less (after adjustment) than the control group.

Editor’s Note: The authors suggest several mechanisms for extra virgin olive oil’s anticarcinogenic effect. They observe that while all olive oil provides a high amount of monounsaturated fatty acids (mainly oleic acid) as well as squalene, extra virgin olive oil also provides biologically active compounds that include the polyphenols oleocanthal, oleuropein, hydroxytyrosol, and lignans. The combined effects of oleic acid’s antiproliferative property, squalene’s beneficial effect on intracellular oxidative stress, and polyphenols’ anticancer properties could be responsible for the protection associated with olive oil observed in this study.

* JAMA Internal Medicine. 2015 Sep 14.

Organs Age Differently

Aging may be one thing to your liver and another to your brain, according to research published in Cell Systems.* Researchers compared brain and liver cells of 6-month-old rats to those of 24-month-old animals. They found that aging equally affected immune and stress responses, as well as inflammation. However, metabolic processes were mainly impacted in the liver, and aging mainly affected signaling processes in the brain.

“We chose to compare brain and liver because these two organs have very different capacities for self-renewal,” stated co-corresponding author Martin Hetzer.

“We found that in the brain, age-related changes very often have to do with the loss of molecules that help signals to spread among neurons,” reported lead researcher Martin Beck. “This could explain why old rats have a reduced ability to form new connections between neurons, as well as other traits observed in the aging brain.”

Editor’s Note: “This research may shed new light on the molecular mechanisms underlying age-related diseases, enabling the identification of risk factors to predict which individuals are most susceptible based on their genetic makeup,” Dr. Beck noted. “In the end, a better understanding of the molecular mechanisms of aging could lead to the development of novel therapies to prevent or treat a range of age-related diseases.”

* Cell Systems. 2015 Sep 17.

Hypertension Drug Reduces Inflammation from Traumatic Brain Injury

According to a new animal study published in The American Journal of Pathology, traumatic brain injury affects the body as well as the brain, and treatment with hypertension drugs blocks the production of proteins related to inflammation.*

Researchers from the Georgetown University Medical Center found that in an animal model, brain injury produces an inflammatory response in the blood as well as body’s organs, especially the liver. The liver responds with up to a 1,000-fold increased production of a protein that increases inflammation in the brain, leading to chronic inflammation, nerve cell death, and reduced blood flow.

In a mouse model, researchers found that small doses of the blood pressure drug telmisartan blocked production of one of the molecules in the protein’s biological pathway, which leads to a dramatic decrease in inflammation. The brain can then possibly heal, says study author Sonia Villapol, PhD.

“This study established a connection between the peripheral regions and the brain, highlighting the importance of regulating the peripheral damage when trying to mitigate the consequences of brain injury,” said Villapol.

In earlier research, the same team found that telmisartan and another hypertension drug, candesartan, had beneficial effects in mice with traumatic brain injury several hours after injury.

Editor’s Note: According to the American College of Cardiology, telmisartan “keeps blood vessels from narrowing, which lowers blood pressure and improves blood flow.” Telmisartan was recommended in the March 2015 edition of Life Extension magazine as the ideal anti-hypertensive medication.

“TURN ON” Your Body’s Longevity Genes!
Optimized Resveratrol with Nicotinamide Riboside for Cellular Vitality

In aging individuals, the accumulation of nonfunctional cells parallels a decline in natural immune function, which is linked to problematic outcomes in normal aging.¹

Scientists have found that the flavonol quercetin supports the body’s normal ability to perform “cellular housekeeping” to selectively break down these nonfunctional cells—promoting their removal.²

**Optimized Resveratrol with Nicotinamide Riboside** now includes 150 mg of quercetin, which is 2.5 times the previous amount.

Quercetin supports cell-regulating systems that produce beneficial apoptosis (cell death) in aged, dysfunctional cells.² It also supports immune response by inhibiting inflammation-causing substances.³

**Optimized Resveratrol with Nicotinamide Riboside** is a complex of key cellular support ingredients formulated to promote the body’s prolongevity mechanisms:

- **Resveratrol** favorably alters genes that help slow the aging process and triggers some of the same beneficial youthful gene expression activated by calorie restriction.⁴
- **Quercetin** enhances the longevity-supporting enzyme SIRT1, which is also activated by both resveratrol⁵ and nicotinamide riboside.⁶
- **NIAGEN® nicotinamide riboside** supports mitochondrial health and promotes longevity pathways.⁵
- **Pterostilbene** and **fisetin**, specific compounds found in berries, work together with resveratrol to “turn on” the body’s own longevity genes.⁷,⁸

Just one vegetarian capsule of **Optimized Resveratrol** provides:

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**For Those Who Want Higher Dose Quercetin**

The new **Optimized Resveratrol with Nicotinamide Ribosome** (described above) provides an ideal daily maintenance dose (150 mg) of quercetin. (Item #02031)

For those seeking to sweep away excess accumulated senescent cells, additional potencies of quercetin may be considered for a two- to four-month period. **Optimized Quercetin** provides 250 mg of a quercetin food blend from apples, onion, and buckwheat. One to two capsules of **Optimized Quercetin** a day may be taken in addition to the Optimized Resveratrol formula over a two- to four-month month period.

Optimized Resveratrol with Nicotinamide Riboside is a complex of key cellular support ingredients formulated to promote the body’s prolongevity mechanisms:

- **Resveratrol** favorably alters genes that help slow the aging process and triggers some of the same beneficial youthful gene expression activated by calorie restriction.
- **Quercetin** enhances the longevity-supporting enzyme SIRT1, which is also activated by both resveratrol⁵ and nicotinamide riboside.
- **NIAGEN® nicotinamide riboside** supports mitochondrial health and promotes longevity pathways.
- **Pterostilbene** and **fisetin**, specific compounds found in berries, work together with resveratrol to “turn on” the body’s own longevity genes.

**Optimized Resveratrol with Nicotinamide Riboside** Item #02031 • 30 vegetarian capsules

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**Optimized Quercetin** Item #01309 • 60 vegetarian capsules

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To order **Optimized Resveratrol with Nicotinamide Riboside** or **Optimized Quercetin**, call 1-800-544-4440 or visit www.LifeExtension.com

References


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.
Replenish Youthful Dopamine

Dopa-Mind™ is a standardized wild green oat extract for aging individuals who wish to maintain more youthful cognitive health and performance.

With age, our brain’s levels of dopamine—which regulates mood and cognition—begin to diminish,\(^1,\(^2\) leading to a corresponding decline in mental performance.\(^3\)

This dopamine depletion is largely caused by rising levels of an enzyme called monoamine oxidase-B (MAO-B).

Published studies show that by inhibiting MAO-B, this bio-active wild green oat extract promotes healthy dopamine levels. This MAO-B inhibiting mechanism has been shown to support mental acuity and longevity.\(^4\)

In a double-blind, randomized, placebo-controlled trial in aging volunteers, researchers demonstrated that 1,600 mg of the same wild green oat extract found in Dopa-Mind™ produced a 74% improvement on a standard test of mental acuity.\(^5\) In soon-to-be published research, 800 mg of the same extract supported mental processing time and speed.\(^6\)

In other research, this extract exhibited support for cerebral vasodilator function, as well as endothelial function—both of which play roles in brain health.\(^6\)

The wild green oat extract in Dopa-Mind™ has been shown to promote more youthful cognitive performance and may support longevity. The suggested dose is one tablet of Dopa-Mind™ daily for the first month. If desired results do not manifest, increase the dose to two tablets daily.

References

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To order Dopa-Mind™, call 1-800-544-4440 or visit www.LifeExtension.com
AMPK ACTIVATOR

A PARADIGM IN CONTROLLING AGING

Found in every cell,12 AMPK promotes longevity factors that have been shown to extend life span in numerous organisms.3,4 Increasing AMPK signaling “turns off” many damaging effects of aging, thus enabling cells to return to their youthful vitality.5

Importance of AMPK

Studies show increased AMPK activity supports reduced fat storage,6 new mitochondria production,7 and the promotion of healthy blood glucose and lipids already within normal range.4

Gynostemma Pentaphyllum

An extract of the plant Gynostemma pentaphyllum promotes AMPK activation8-10 In one of many studies showing a wide variety of benefits, researchers documented a 1-inch reduction in abdominal circumference in overweight individuals who took 450 mg daily of G. pentaphyllum extract for 12 weeks.11

Trans-Tiliroside

Trans-tiliroside, extracted from plants such as rose hips, boosts AMPK activation, but triggers different downstream metabolic benefits than G. pentaphyllum.12-14 Among its many benefits, a low equivalent dose of 56 mg daily trans-tiliroside has been shown by researchers in preclinical studies to promote healthy blood glucose levels and body weight already within normal range.15

Activate Your AMPK!

Over 7,500 published studies document the role that AMPK plays in protecting critical cellular functions. Those seeking healthy aging should prioritize re-activating their AMPK cellular enzyme.

AMPK Activator provides nutrients shown to significantly boost AMPK activity. The suggested daily dosage of AMPK Activator is to take two capsules with the first meal of the day and one capsule with the second meal. Three capsules provide:

ActivAMP®

Gynostemma pentaphyllum extract 450 mg
Rose hip extract 1,119 mg
Standardized to 5% trans-tiliroside 56 mg

References:
4. Physiol Rev. 2008;89(3):525-78.

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To order AMPK Activator, 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.
INNOVATIVE SOLUTION FOR ORAL HEALTH
For many people, strict adherence to brushing and flossing twice daily may not be enough. The consequence is deterioration of gums and teeth with invariable periodontal disease.\textsuperscript{1,2}

Researchers have discovered a unique solution to ensure healthier gums and teeth as we age. It comes in the form of a targeted probiotic that has been found to work specifically in the mouth. This unique probiotic helps destroy disease-causing bacteria and replaces them with beneficial bacteria that protect teeth and gums.

In a revealing human study, subjects receiving the oral probiotic showed an impressive reduction in indicators of plaque buildup, gingivitis, bleeding gums, and pocket depth between gums and tooth roots.\textsuperscript{3}
Americans have an alarmingly high rate of gum disease. Beyond the potential for tooth loss, gum disease is associated with health problems throughout the entire body, including cardiovascular, brain, kidney, and bone diseases.4,10

A major factor in the development of tooth and gum disease is an imbalance in the normal oral microbial community of the mouth, in which disease-causing organisms overwhelm those that contribute to good health.

Researchers have discovered a targeted oral probiotic that is able to “safeguard” the oral cavity, help minimize bad bacteria, and replace it with beneficial bacteria instead.

Studies have shown that oral probiotics improve gum health and reduce risk factors for dangerous periodontal (gum) disease. That risk reduction, in turn, translates into substantially lower risk for a host of systemic disease processes commonly associated with aging.11

**How Oral Health Impacts the Entire Body**

Disorders involving the teeth are among the most common health problems in US adults, with 96% of those 65 and older having cavities in their permanent teeth and about 20% of adults 65 and older having untreated tooth decay.12

Periodontal (gum) disease is an even more serious and potentially dangerous problem in aging adults.13 More than 70% of adults 65 and older have periodontitis, a term that includes a range of conditions from simple gingivitis (inflammation of the gums without destruction of bone or tooth structures) to aggressive periodontitis, which can lead to bone loss, weakening of the ligaments that hold teeth in place, and eventual tooth loss.

The consequences of periodontal disease are grave, and considerably more threatening than dental cavities. And, while many have to face the expense of dental work or dentures, tooth loss alone can lead to serious malnutrition as the act of chewing becomes increasingly difficult.14,15

What many people might not know is that periodontal disease is a major threat to health throughout the body.10,16

The degree of periodontal inflammation and the presence of pathogenic bacteria has long been linked to coronary artery disease and atherosclerosis.4,17-19 Periodontal pathology also contributes to:

- **Cancers** of the oral cavity and other regions caused chronic infections and inflammation.5,6
- **Alzheimer’s disease** and other forms of dementia as a result of inflammatory changes. Accumulation of neuron-destroying amyloid beta increases in adults with periodontal disease.16,20
- A variety of **lung disorders**, which are associated with periodontal disease, including pneumonia and chronic obstructive pulmonary disease (COPD).21-23
- **Nonalcoholic fatty liver disease (NAFLD)** and **viral hepatitis**, which are likely to be associated with inflammatory periodontal disease.24,25
- **Kidney diseases**, including renal insufficiency and chronic kidney disease, show close associations with periodontal problems.26,27

**The Underlying Cause of Gum Disease**

How can something as seemingly simple as gum disease have such potentially drastic health effects throughout the body? The answer comes down to one of the underlying causes of gum disease, which is the excessive growth of pathogenic (disease-causing) organisms in the oral cavity. This creates the twin threats of infection and inflammation, which feed on each other in a vicious cycle and can have disastrous effects on many body systems.28
Present in everyone, the oral microbiome, is a complex set of interacting microbial populations, which, when in a healthy balance, support and protect the delicate mucous membranes as well as the surfaces of the teeth themselves.29

Shifts in the normal microbial community, however, lead to a host of problems, ranging from dental caries (“cavities”) that arise from excessive acid-producing bacteria, to gum disease that contributes to tooth loss and diseases in parts of the body far removed from the mouth itself.30

Our growing recognition of both the severity of periodontal disease and its relationship to an imbalance in the oral microbial populations have led to calls for use of oral probiotics as effective preventive measures, in an effort to re-establish a healthy microbial community in the mouth.30,31 The results are extremely promising.

Beneficial Organisms Destroy Dangerous Germs

The principle behind all probiotics is simple: Replace unhealthful or dangerous organisms with those that contribute directly or indirectly to human health. The end result should be a reduction in the population of the “bad guys,” and the establishment of a more protective environment.

*S. salivarius* strain BLIS M18 is one of the “good guys.” It competes with dangerous oral bacteria that cause or exacerbate periodontal disease, and has been shown to prevent and improve parameters of gingivitis and periodontitis.9 It accomplishes this through numerous mechanisms of action.

First, *S. salivarius* produces enzymes that help break down dental plaque, which is a major threat to both tooth and gum health.32 Plaque is the sticky film of bacteria that forms on teeth, and it's the main cause of tooth decay and gum disease. When plaque hardens, it becomes tartar, a mineralized substance with a rough surface that can become home to still more plaque and more dangerous microbes.

Another benefit of *S. salivarius* is that it has been shown to neutralize acids to maintain a healthy oral pH. A healthy oral pH is important because having a low pH demineralizes teeth, which creates an environment in which bad bacteria thrive.32,33

**What You Need to Know**

**Oral Probiotic for Gum Disease**

- Poor oral health is common among US adults, with the bulk of the impact on older adults.
- Poor oral hygiene leaves individuals vulnerable to an imbalance of the billions of microbes living in our mouths, allowing formation of plaque, development of inflammation, and eventually gum disease and tooth loss.
- As gum disease (periodontitis) progresses, it can have disastrous effects on other organ systems, including the heart, brain, lungs, kidneys, and bones, as a result of the chronic, low-grade inflammation it causes.
- Rebalance oral microbial population through the use of a novel probiotic bacterial strain, *S. salivarius* BLIS M18.
- Studies show that regular supplementation with *S. salivarius* BLIS M18 results in significant improvements in measures of oral and gum health.
- The addition of a second probiotic organism, *Bacillus coagulans* GBI-30, 6086, provides extra support against the germ most commonly associated with dental caries.
- Oral health is much more than a cosmetic consideration. To sustain healthy teeth, gums, and total body health, it’s time to include a daily supplement with these powerful beneficial probiotic organisms.
Laboratory studies show that colonies of *S. salivarius*-producing lantibiotics can inhibit the growth of oral disease-causing bacteria associated with periodontitis.37,39

One important study showed that in addition to inhibiting the growth of dangerous bacteria, *S. salivarius* BLIS M18 can also reduce levels of inflammatory cytokines associated with gingivitis and periodontitis.41 This is an important characteristic in breaking the infection-inflammation-infection cycle that accelerates gum disease and threatens the rest of the body.

**Oral Probiotic Improves Gum Disease**

Once scientists knew that oral probiotics produced such beneficial antibacterial actions in lab and preclinical studies, they were ready to test their effects in real life. A number of human trials have now been completed, with exciting results that demonstrate the positive impact of regular supplementation with an oral probiotic.

A randomized, controlled clinical trial was conducted to determine the effects of *S. salivarius* BLIS M18 on a number of the most important clinical parameters of periodontal health. This study evaluated indicators that dental hygienists use to determine the health of gums:9

- **Plaque index score**: a 0-to-3 scale ranging from no plaque to an abundance of soft matter within the gingival pocket (the pocket of soft tissue between gum and tooth).42
- **Gingival index score**: a 0-to-3 scale ranging from normal gingiva (gums) to severe inflammation with marked redness and swelling, including ulceration and tendency of spontaneous bleeding.43
- **Sulcular bleeding index**: a 0-to-5 score grading tendency of the gums to bleed on probing, ranging from healthy-looking gums with no bleeding on probing to spontaneous bleeding, change in color, and marked swelling.43
- **Probing pocket depth**: the depth to which a dental probe can be passed between the inner margin of the gum and the tooth root. The deeper the pocket depth, the worse the evidence of periodontal disease.44

The study involved both male and female patients with moderate and severe gingivitis (scores of 2 or 3 on gingival index score), and moderate periodontitis.37,38
Further Reduce Tooth Decay and Inflammation

A companion organism has been identified that provides additional oral health support to *S. salivarius* BLIS M18. This probiotic strain called *Bacillus coagulans* has been shown to competitively inhibit the growth of *Streptococcus mutans*, a bacterium that contributes to tooth decay.45

A patented strain of this organism, GBI-30, 6086 (GanedenBC30®) helps increase the body’s natural resistance to pathogenic organisms by boosting the immune system and reducing production of inflammatory cytokines that promote the inflammatory response.46

Summary

Poor oral health is widespread among maturing individuals, with the highest rates of gum disease prevailing among older adults. Gum disease leads to tooth loss and expenses related to dental work and dentures. Worse than tooth loss, however, are the total body health implications of gum disease. The chronic presence of inflamed tissue contributes to the chronic, low-grade inflammation associated with so many of the disorders we associate with aging, including cancer, cardiovascular, brain, kidney, and bone diseases.
A major factor in the development of tooth and gum disease is an imbalance in the normal oral microbial community of the mouth, in which disease-causing organisms predominate and sideline those that contribute to good health.

By rebalancing the oral microbial community with *S. salivarius* strain BLIS M18, individuals can turn the tables on the pathogens in the mouth, marginalizing them and allowing healthy organisms to predominate. This natural probiotic strain produces powerful *lantibiotics*, which are germ-killing molecules that act locally within the mouth to suppress more harmful germs.

Studies show that regular supplementation with *S. salivarius* BLIS M18 can improve multiple measures of gum health and reduce inflammation in the oral cavity. Further inflammation control is provided by addition of beneficial *Bacillus coagulans* another probiotic strain that inhibits the germs that cause dental caries and helps to reduce the inflammatory response.

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

**Suggested Usage**

To emulate the successful clinical findings described in this article, make an appointment with your dentist for a thorough cleaning and scraping of your teeth to remove plaque and tartar. This will help reduce colonies of dangerous bacteria your mouth harbors.

Then immediately initiate daily use of a lozenge containing *S. salivarius* and *Bacillus coagulans*.

Based on the clinical study results, some people may only need to use this lozenge every other month.

Those with serious oral health issues should consider using the lozenge continuously at least until clinical and symptomatic improvements in oral health manifest.

The objective is to rebalance the communities of bacteria that live in your mouth, promoting not just improved oral health, but the health of the entire body.
References


Bone density loss is more than just a calcium deficiency—it also includes an insufficient intake of a host of other nutrients.

**Bone Restore** combines numerous bone-boosting nutrients into one superior, easy-to-take formula. In addition to **700 mg** of **highly-absorbable** calcium, **Bone Restore** provides meaningful potencies of:

- Boron
- Vitamin D3
- Magnesium
- Manganese
- Zinc
- Silicon

These nutrients work together to keep aging bones strong.

**Bone Restore** also contains **vitamin K2**, which has been shown to play a critical role in maintaining healthy bone density by facilitating the transport of calcium from the bloodstream into the bone.

**Who Should Take Bone Restore**

Progressive **loss of skeletal density** is a consequence of normal aging. Fortunately, an array of **nutrients** has been identified that can markedly impede and sometimes reverse this degenerative process.

**Bone Restore** is designed to provide the best forms of these nutrients in ideal potencies. It contains the **MK-7** form of **vitamin K2**. Many readers of this publication already obtain MK-7 in the **Super K** or **Health Booster** (formerly called **Super Booster**) formulas. For these individuals, **Bone Restore** is available without vitamin K2. The retail price for this formula of 120 capsules is **$22**. If four bottles are purchased during Super Sale, the price is reduced to **$12.85** per bottle. (Item# 01726)

Non-GMO

**Note:** Those taking the anticoagulant drug Coumadin® (warfarin) should use **Bone Restore** without vitamin K2.

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**Bone Restore with Vitamin K2**
Item #01727 • 120 capsules

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To order **Bone Restore**, call 1-800-544-4440 or visit www.LifeExtension.com

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Regular brushing and flossing is often not enough to achieve optimal oral health. Since the mouth is the major gateway to the body, maintaining good oral hygiene is important for overall health.¹

Researchers have developed an innovative approach to achieving maximum oral health. The beneficial bacteria in FLORASSIST® Oral Hygiene helps inhibit harmful bacteria that develop in the mouth and can affect the health of your teeth and gums. FLORASSIST® Oral Hygiene complements any oral care program.

FLORASSIST® Oral Hygiene contains a unique blend of two powerful oral probiotics:

- The beneficial probiotic strain—S. salivarius BLIS M18™
- An additional healthy probiotic—B. coagulans GanedenBC30®

FLORASSIST® Oral Hygiene provides healthy bacteria that colonize the mouth and inhibit the growth of problematic mouth bacteria.² This helps create a healthy environment in the oral cavity.

Because FLORASSIST® Oral Hygiene comes in lozenge form, it quickly provides healthy, targeted probiotics to the oral cavity.

Dissolving one lozenge of FLORASSIST® Oral Hygiene in your mouth daily can maximize your oral health by optimizing oral pH, easing inflammation, and supporting healthy bacterial colonization throughout the mouth.³ ⁴

To order FLORASSIST® Oral Hygiene, call 1-800-544-4440 or visit www.LifeExtension.com

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As humans age, proteins in their bodies become damaged by glycation reactions. Glycation can lead to alterations of normal cell function. Carnosine is a powerful anti-glycating agent, and protects neurons against reactive and cytotoxic protein carbonyl species associated with normal aging.2,7

This free amino acid supports whole-body health and boosts new brain cell formation.2

MITOCHONDRIAL ENERGY OPTIMIZER

Back in year 2001, we at Life Extension® faced a dilemma. Potent nutrients had been discovered to counteract undesirable age-related changes. Yet the cost of the individual ingredients was too high. So we combined these nutrients into one formula so consumers could obtain them at an affordable price.

Over the years, the published data about the amino acid taurine has grown enormously. In addition to protecting cardiac function, taurine has demonstrated powerful brain-boosting effects that include enhancing neurites and promoting new brain cell formation.2

These new findings indicate that taurine is more important to supplement with than acetyl-L-carnitine arginate. In addition, taurine costs much less than acetyl-L-carnitine arginate.

So we’ve re-formulated the popular Mitochondrial Energy Optimizer using taurine and reduced the retail price over 20%. Aging is characterized by inflammation, glycation, mitochondrial decay, and loss of cellular structure/function. Mitochondrial Energy Optimizer provides the following nutrients to help neutralize these changes:

- CARNOSINE: As humans age, proteins in their bodies become irreversibly damaged by glycation reactions. Glycation can lead to alterations of normal cell function. Carnosine is a powerful anti-glycating agent, and protects neurons against reactive and cytotoxic protein carbonyl species associated with normal aging.2,7
- PQ: This micronutrient has been shown to trigger the growth of new mitochondria in aging cells! PQ also activates genes involved in protecting the delicate structures within the mitochondria.9-12
- LUTEOLIN: Systemic inflammation is involved in most consequences of aging. Cytokins behind inflammatory reactions are pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha. Luteolin is a flavonoid that has been shown to help suppress these inflammatory cytokines.15-17
- BENFOTIAMINE: Benfotiamine blocks multiple destructive biochemical pathways, including AGES’ formation pathway, which is induced by higher than desirable blood glucose levels. Benfotiamine can activate glucose metabolism and promote already healthy blood glucose levels. In addition, benfotiamine exhibits direct antioxidant capacity and supports DNA function.24
- PYRIDOXAL 5’-PHOSPHATE: Aging results in the formation of advanced glycation end products throughout the body. Pyridoxal 5’-phosphate is the active form of vitamin B6 that has been shown to protect against both lipid and protein glycation reactions.25-28
- R-LIPOIC ACID: Destructive free radical activity in the mitochondria plays a major role in the loss of cellular vitality. A microencapsulated Bio-Enhanced® R-lipoic acid facilitates youthful mitochondrial energy output while guarding against free radicals.29,33
- TAURINE: This free amino acid supports whole-body health and boosts new brain cell formation in the area of the brain connected to learning and memory.1

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

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CoQ10 Energizes Aging Cells by Enhancing Mitochondria Activity

Published studies on CoQ10 absorption clearly show that ubiquinol CoQ10 is superior to the conventional ubiquinone form. In middle-age mice, ubiquinol proved 40% more effective in slowing measurements of aging compared to ubiquinone.1

A 2014 study further validates that ubiquinol activates mitochondrial functions to slow aging in mouse models.2

Life Extension® goes one step further and adds shilajit to its ubiquinol formula in a product called Super Ubiquinol CoQ10. Shilajit has been shown to promote mitochondrial metabolism, helping mitochondria convert fats and sugars into ATP—the main source of cellular energy.3-8 When combined with ubiquinol, it has been shown to double levels of CoQ10 in the mitochondria.9

The latest studies reveal that when shilajit is combined with CoQ10, cellular energy substantially increases. Combining the two ingredients produced a 56% increase in energy production in the brain—40% more than CoQ10 alone! In the muscles, there was a 144% increase.10

References

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STOP ACCELERATED AGING!

The Importance of Rebuilding the Immune System
A major factor underlying *accelerated aging* is a phenomenon known as *immune senescence*. This marked decline in *immune function* strikes as we age past 60 years and leaves us vulnerable to a host of opportunistic diseases.

Not only do we lose the ability to defend against cancers and infections, but our failing immune cells create a state of *hyper-inflammation* that destroys neurons, endothelium, and joints.\(^1,2\)

**Life Extension**\(^\circ\) is funding research projects aimed at reversing the immune imbalance that causes chronic inflammatory disorders while failing to protect us from common pathogens. Once this research becomes clinically available, it may be possible to restore immune function back to youthful functionality.

The encouraging news is that maturing individuals can initiate steps today to improve immune surveillance while suppressing the degenerative fires of chronic inflammation.
Immune senescence makes us vulnerable to all the diseases of aging.

Recognition of this universal disorder has motivated scientists to identify solutions to compromised immune function through innovative pharmaceuticals and gene therapies. The dilemma is that translating these advances into clinical practice is still a few years away.

Fortunately, researchers have identified three specific natural compounds that have each been shown to reverse a broad spectrum of harmful changes that occur in the immune system with advancing age.

These three compounds are extracts of Pu-erh tea, Cistanche, and Reishi mushrooms.

Each of these natural compounds has a millennia-old history in traditional Asian medical systems, and is prized for their properties of improving quality of life and health, while promoting longevity. Each one also has its own unique profile of immune system-modulating effects that directly oppose the pathologic components of immune senescence.

Together, these nutrients help put the aging immune system back on a more youthful track, which in turn should help lower the risks for infections, malignancies, autoimmune disorders, and chronic inflammation.

How Aging Affects the Entire Immune System

Young people have a vigorous and well-regulated immune system that constantly patrols the body in search of potential threats to the healthy functioning of the body.3

But as people age, the immune system begins to lose its potency and effectiveness1,2 in a process called immune senescence. This aging in the immune system results in potentially devastating loss of the three main weapon systems against foreign invaders and cancer cells:

1. Reduction of bone marrow production of immune system cells,
2. Reduction of the supply and potency of circulating immune cells, and
3. Loss of control over the production of the inflammatory and anti-inflammatory cytokines that maintain a safe and natural balance between sufficient and excessive inflammation.

As a result of these three changes, older adults become much more vulnerable to genuine threats, such as bacteria, viruses, and cancers, and at the same time are more likely to succumb to autoimmune disorders.1

Immune senescence can lead to a constant inflammatory state, in which the immune system is always “on” and often ends up attacking the body. This vicious cycle raises the risk for chronic conditions associated with aging, including arthritis, atherosclerosis, osteoporosis, and cancers.1

The good news is that extracts of Pu-erh tea, Reishi mushrooms, and Cistanche can help us fight back against the various factors of immune senescence. As beneficial as each individual component is, they have overlapping immunomodulatory activities that make the sum greater than the parts.

This article examines the immune benefits of each ingredient.

Pu-erh Tea Extract

Pu-erh tea (fermented, ripened leaves of Camellia sinensis) was historically prescribed to the emperors of China to provide them with longevity. It is native to the Upper Mekong River region of China’s Yunnan province, a land of rain forests, rushing mountain rivers, and some of the world’s most spectacular scenery.

A major new study shows that Pu-erh tea extract contributes to reversing multiple components of immune senescence.

The study involved a widely used animal model of human aging, the senescence-accelerated mouse strain P8, or SAMP8 mouse.4 These SAMP8 mice are ideal for this kind of study because they have a shorter life span than normal mice and they demonstrate all of the immunological dysfunction seen in human immune senescence.
For the study, male SAMP8 mice and control mice that had normal aging and life spans were given either oral supplements of Pu-erh tea extract at various doses or a placebo for 28 days. The animals’ blood was then tested for various markers of immune dysfunction.

At the beginning of the study, the age-accelerated mice showed all of the features of immune senescence that occur in humans. For example, they had significantly lower bone marrow production of the vital stem cell antigen-1 (Sca-1), a cell marker that indicates a robust, active production of healthy white blood cells. They also had lower proportions of versatile naïve T cells, natural killer cells, and activated cytotoxic T cells, while memory T cells were higher, as would be expected. In addition, levels of the powerful pro-inflammatory cytokine IL-6 were markedly elevated in the senescence-accelerated mice, compared with controls.

After supplementing with Pu-erh tea extract for four weeks using a dose equivalent in humans to 650 mg per day, all of these features were reversed:

- In bone marrow, the proportion of Sca-1 stem cells rose approximately 42%, suggesting a much broader and faster immune response to challenges.

- In circulating white blood cells, the proportion of natural killer (NK) cells rose by an approximate 7%, while the percentage of versatile naïve T cells had an increase of about 10%, and the proportion of activated T cells rose close to 9%. This increase indicates enhanced protection against viral infections and cancers.

- IL-6 levels, a pro-inflammatory cytokine, fell by a significant 43%, reducing the risks associated with high IL-6 and chronic inflammation.
Powerful Anti-Inflammatory Effects in Humans

A human study of Pu-erh tea extract further emphasizes its role in reversing inflammatory cytokine levels. The study was performed among a group of patients with metabolic syndrome, a common condition defined by central obesity, borderline or high fasting glucose, and elevated triglycerides and cholesterol. Those with metabolic syndrome have higher levels of inflammation and are at an increased risk of having low naïve and high memory T cell populations.

Subjects were given either Pu-erh tea extract twice daily or a placebo. They were instructed to exercise and observe a healthy diet during the study period, but were permitted no medicines that might otherwise affect the results. After three months, patients provided blood samples for analysis of inflammatory cytokines and other markers of inflammation.

As expected, placebo recipients showed no significant changes in blood levels of TNF-\(\alpha\) or IL-6 (pro-inflammatory cytokine), IL-10 (an anti-inflammatory cytokine), or C-reactive protein (CRP, a marker of total body inflammation).

Subjects supplemented with Pu-erh tea extract showed robust improvements in immune status, including a marked reduction in inflammatory markers such as:

- 21% reduction in IL-6,
- 23% reduction in TNF-\(\alpha\),
- 26% reduction in CRP, indicating significant decreases in their overall inflammatory status, and
- 34% increase of inflammation-quelling IL-10, further demonstrating the overall reduction in inflammation.

Clearly, Pu-erh tea extract offers multiple benefits to prevent the progress of immune senescence. But, just as a good roof provides multiple, overlapping structures to prevent leaks, good immune system coverage should offer multiple, overlapping mechanisms to ensure that no possible holes are left to allow untimely infections, inflammation, or cancers to progress.

As we will now see, Reishi mushrooms provide an ideal complement to Pu-erh (pronounced “Poo-air”) tea extract.

### Skyrocketing Death Risks with High Levels of IL-6 and CRP

<table>
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<td><strong>IL-6</strong></td>
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<td>Increased risk of dying from any cause in people with a mean age of 61(^{65})</td>
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<td>Increased risk of dying from any cause in people older than 80(^{66})</td>
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<td>Increased risk of death following acute heart attack(^{67})</td>
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<td>Increased risk of sudden cardiac death(^{68})</td>
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<td>Increased risk of dying from any cause in patients with obstructive airway disease(^{69})</td>
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<td>Increased risk of congestive heart failure following acute heart attack(^{67})</td>
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<tr>
<td>Increased risk of poor functional outcome after stroke(^{70})</td>
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<td>Increased risk of knee osteoarthritis(^{71})</td>
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<tr>
<td>Increased risk of developing the blindness-inducing eye disease age-related macular degeneration (AMD)(^{72})</td>
<td>78%</td>
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Reishi Mushrooms Teach Cells about Antigens, Antibodies

Reishi mushrooms (Ganoderma lucidum) have long been used in traditional Asian medical systems for the prevention and treatment of numerous human diseases.7 These myriad benefits stem from Reishi’s multiple classes of bioactive molecules, including polysaccharides, triterpenoids, sterols, and alkaloids. Each of these different components has a slightly different mechanism of action, resulting in very broad-spectrum immune system coverage.7

Like Pu-erh tea extract, Reishi extracts resurrect youthful patterns of circulating white blood cells, including NK and T cells.8-10 Reishi also helps raise protective IL-10 levels and lower pro-inflammatory IL-6 levels in animal studies.11,12

However, while Reishi lacks the bone marrow-stimulatory effects of Pu-erh tea extract, it has other benefits that Pu-erh tea does not, such as stimulating activities of immune circulating cells and stimulating energy production and transfer required by the frenetic metabolic activity of active immune cells.13

In addition, Reishi enhances numbers and activities of the B cells. These B cells make antibodies and the macrophage/monocyte line of cells that engulf and destroy bacterial invaders. B cells also process foreign molecules (antigens), “presenting” them to T and B cells as examples of enemies in need of destruction.7,9,14-18

In this way, Reishi exerts subtle but powerful effects that reverse many of the impacts of immune senescence.1

Reishi Protects against Deadly Microorganisms

Based on laboratory and animal studies, there’s now evidence that Reishi’s cellular and molecular mechanisms directly protect against a deadly array of microorganisms that threaten the health of aging individuals. More human studies need to be done, but based on a number of published studies the potential benefits of Reishi are extremely promising.

- Components in Reishi have been found to block infection with Herpes simplex (the virus that causes cold sores and genital herpes) and Herpes zoster (the virus responsible for painful shingles infections).19 They accomplish this by activating natural killer cells and stimulating their proliferation, triggering them to label and destroy cells infected with the virus,19 and by directly binding to the viruses, preventing them from attaching to and penetrating healthy body cells prior to setting up an infection.20

- Reishi extracts have been shown to reduce the painful effects of the viral outbreak in patients with postherpetic neuralgia, an excruciating condition often resistant to standard pain management.21 As with so many natural therapies, Reishi is most effective against herpes viruses when it is administered prior to the outbreak infection.20,22

- Influenza viruses are also targets of Reishi mushroom extracts, which are rich in trace elements essential for preventing influenza infections and mitigating their severity.23

- Reishi extracts potently inhibit the Epstein-Barr virus,24,25 which causes both the relatively mild mononucleosis in young people and also several kinds of aggressive lymphomas in older ones.26

- Reishi mushroom extracts are effective against the dangerous hepatitis B virus (HBV), a major cause of liver disease worldwide. Studies show that the extracts can inhibit viral replication, reducing the organism’s ability to express itself in liver cells.27,28

- Finally, Reishi extracts have an important role in combating one of the major scourges of the modern world, the human immunodeficiency virus (HIV), which causes the acquired immune deficiency syndrome (AIDS). Reishi extracts produce a dramatic drop in the viral “load” (number of active virus particles) in monkeys infected with simian acquired immune deficiency syndrome (SAIDS), a model of human HIV/AIDS disease.29 Laboratory studies now demonstrate that active compounds from Reishi mushrooms act by inhibiting HIV enzymes called proteases, an action identical to that of some of the most successful anti-HIV drugs on the market, but with vastly lower toxicity.30 In this context, Reishi mushrooms have been said to have “huge potential for HIV drug discovery.”30

All of these actions ultimately reflect the importance of Reishi mushroom extracts in reversing immune senescence by strengthening the aging immune system, while at the same time exerting direct destructive effects against some of humanity’s most relentless microbial foes.

But the beneficial effects of these remarkable mushrooms go still further, into the complex world of cancers and their interactions with the immune system.
STOP ACCELERATED AGING!

Cistanches Enhances Immune Responses

Cistanche deserticola is a resilient desert plant commonly used in traditional Chinese medicine to enhance longevity and treat many different health problems.\(^3^8\) Cistanche extracts have been found to combat immune senescence by enhancing healthy immune responses while suppressing deleterious inflammatory ones.

Its extracts reduce inflammatory changes in animal models of intestinal inflammation, while also boosting the numbers of circulating white blood cells such as macrophages (“eating cells”) and NK cells, particularly in the spleen, in ways that Pu-erh tea extracts do not, though this activity does overlap constructively with that of Reishi.\(^3^8,^3^9\)

Cistanche supplementation in animals also increases numbers of versatile naïve T cells, and reduces numbers of inflexible, committed memory T cells, while lowering pro-inflammatory IL-6 levels in blood.\(^3^9\) Cistanche stimulates bone marrow production of white blood cells, an effect found in Pu-erh tea extract, but lacking in Reishi.\(^3^9\)

But there’s one additional compound called Cistanche that adds still another layer of immune system-potentiating proprieties.

Reishi Combats Cancer

Reishi mushroom extracts help prevent cancer before it starts by activating and modulating patrolling T cells and natural killer cells. These are the cells that identify abnormal cancerous tissue and attack it before it has a chance to develop into a full-blown tumor.\(^3^1,^3^2\) This is primarily the result of interactions of Reishi polysaccharide molecules with immune system cells, especially those in the spleen and the thymus, both of which are sources of aggressive cancer-killing cells.\(^3^3-^3^5\)

In mice bred to carry human cancers, Reishi has been found to inhibit tumor growth and prolong life span by stimulating normal immune function. Importantly, this effect was seen even when the animals were treated after tumors had developed.\(^3^6\)

A similar extract of Reishi polysaccharides was found to markedly increase the ability of immune system cells to proliferate, engulf, and destroy tumor cells in mice bearing a variety of human cancers.\(^3^4\) In addition, Reishi polysaccharides have been found to inhibit the adhesion of the “coating” protein, fibrinogen, to cancer cells, thereby stripping malignant cells of the protection naturally afforded by fibrinogen, and making the cells directly accessible to NK cells that destroy them.\(^3^7\)

With all of this evidence in hand, it is easy to see why Reishi mushroom extract makes an ideal companion to Pu-erh tea extract in providing broad-spectrum protection aimed at preventing and reversing immune senescence and its infectious and malignant consequences.
Cistanche’s anti-inflammatory effects deserve some additional notice, given the importance of inflammation in most age-related diseases. Increased inflammation itself is a clear-cut consequence of immune senescence, as the body’s immune regulatory systems begin to fail, releasing pro-inflammatory processes from their normal, youthful levels of control.

In animal studies, supplementation with Cistanche extracts reduces the inflammatory overgrowth in the intestines of cancer-prone mice (these animals, like humans, develop increased intestinal inflammation prior to development of cancers). And Cistanche components known as phenylethanoid glycosides have been credited with multiple anti-inflammatory actions through their impact on a host of inflammatory molecular processes.

These unusual molecules have been shown to have the following anti-inflammatory actions:

- Inhibition of pro-inflammatory signaling.
- Reduced production of inflammatory cytokines including TNF-α and IL-4.
- Reduced allergic responses related to decreased production of histamine and other contributors to allergy, which is in essence an inflammatory overreaction of the immune system.

Cistanche Increases Life Span

The combination of Cistanche’s ability to enhance healthy immune responses while suppressing deleterious inflammatory ones has been credited with extending life span in mouse models of aging. Here are the intriguing details.

A group of Chinese researchers used a special strain of laboratory mice bred to age faster than normal mice (the same SAMP8 mice mentioned earlier), to study the effects of Cistanche supplementation on life span. The accelerated aging of these animals produces accelerated immune senescence as well. The first finding in this study was significant reductions in the supplemented animals’ “memory T cells,” which are immune system cells that can only respond to one kind of threat that they have experienced in the past. An increased proportion of senile memory T cells is a classic feature of immune senescence because these cells have lost their flexibility to respond to new threats.

At the same time, Cistanche-supplemented mice had increased numbers of so-called “naïve T cells,” which are immune cells that have not yet encountered any threat, and are therefore capable of rapid responses to any abnormal cell, such as an infecting organism or a potentially cancerous cell.
Cistanche-supplemented mice also had increased numbers of natural killer (NK) cells, which respond to T cell signals and apply the death blow to the new invader. One of the most exciting features of this study is the impact of Cistanche supplementation, and the reversal of immune senescence, on the animals’ life spans.

In this study, while control mice lived on average about 325 days, mice supplemented with Cistanche lived to an average of about 375 days. That’s a 15.4% increase in life span (See Figure 1). If this increase were applied to the human life span, the average American female’s life expectancy would jump from 81 to more than 93 years, while that of the average American male would jump from 76 to 88 years.5

Read the preceding paragraphs again carefully, and you’ll discern the emergence of a new paradigm for fighting aging. In addition to focusing on preventing or repairing heart disease, Alzheimer’s disease, stroke, cancer, and other disease processes that shorten life span, an overall improvement in the immune function seems capable of promoting longevity all by itself!

**FIGURE 1: Life Span Extension in Mice Supplemented with Cistanche.**

A) Cistanche increased survival of age-accelerated mice. Control mice (green line) were all dead by about 382 days, and low-dose (pink) Cistanche mice had all died by about 413 days. About 5% of mice supplemented with medium (blue) and about 10% of mice supplemented with high (gold) doses of Cistanche were still alive by the end of the study, at 425 days.

B) Cistanche increased average life span of mice. Control age-accelerated mice (blue) lived on average about 325 days, as did mice supplemented with low-dose Cistanche (green). Mice supplemented with medium (yellow) and high (red) doses of Cistanche, however, had longer life spans compared with control mice, at about 350 and 375 days, respectively.5
Summary

Immune senescence is a consequence of normal aging. It is a major cause of the ill effects associated with growing older.

Immune senescence is accompanied by the devastating loss of three main weapons systems against foreign invaders and cancer cells including:

1. **Bone marrow** production of immune system cells.
2. Potency of **circulating immune cells**.
3. Control over **signals** that maintain a youthful balance between sufficient and excessive inflammation.

The cumulative impact of **immune senescence** is seen in the high rates of infections and cancers, the poor response to vaccines, and the chronic inflammatory state that predominates among older adults who might otherwise be in excellent health.

It’s now possible to fight back against immune senescence with help from three natural ingredients. Extracts of **Pu-erh** tea, **Reishi** mushrooms, and **Cistanche** have demonstrated their own suite of immune senescence-fighting properties that help restore more youthful immune function.

Maturing individuals face health threats posed by immune senescence. Major breakthroughs may be around the corner, but taking steps now to rebuild aging immune systems is a critical component of a science-based longevity program.

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**References**


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(References continue on page 45.)

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### Overlapping Immunomodulatory Activities of Three Natural Extracts

<table>
<thead>
<tr>
<th>Extract</th>
<th>Stimulates Bone Marrow</th>
<th>Stimulates Circulating White Blood Cells</th>
<th>Lowers IL-6 Levels</th>
<th>Boosts IL-10 Levels</th>
<th>Enhances Antibody Production</th>
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(References continue on page 45.)
The following is a more detailed look at the three aspects of the immune system that are positively impacted by Pu-erh tea, Reishi, and Cistanche extracts. Scientists have now identified many of the specific problems that occur during immune senescence. These problems arise in all three of the immune weapons systems.1,2

Bone Marrow

Bone marrow is where circulating white blood cells are made, along with red cells that carry oxygen and platelets that stop bleeding.54 All bone marrow-derived cells originate from a common predecessor, the blood-forming stem cells that differentiate into a wide variety of circulating white blood cells, with a bewildering array of names and functions.

Immune senescence causes a reduction in bone marrow stem cell activity, leaving us with reduced numbers of all the circulating cell lines. Scientists use a cell marker called Sca-1 to measure bone marrow activity in animals: The higher the Sca-1 levels, the more vigorously new white blood cells are being produced. In aging bone marrow, levels of Sca-1 cells fall off significantly, resulting in a sharp, age-related reduction in bone marrow-derived white blood cells and their chemical weaponry, and the subsequent age-associated increase in infections and cancers.55,56 Current animal research has demonstrated valuable stem cell concepts that are relevant to human health and disease.56

Circulating White Blood Cells

Circulating white blood cells are the mature, bone marrow-derived cells that recognize and destroy invading or abnormal cells. Among those most directly affected by immune senescence are natural killer (NK) cells, which directly attack and destroy infecting organisms and tumor cells,1,2,57,58 and a variety of T cells, which are involved in recognizing new threats, remembering old threats, stimulating direct action against invaders or malignancies, and suppressing the immune response appropriately when the invader has been neutralized.59 These cells prevent serious infections, keep a constant patrol out for emerging cancers, and boost immunity after a vaccine.

Immune senescence specifically reduces the numbers and function of fresh young NK cells,1,2,57,58 This is now thought to explain the high rate in older people of many cancers and leukemias, as the malignant cells fly under the impaired NK cells’ radar.1,2,58 In fact, rejuvenation of NK function is being explored as a promising means of preventing the spread of breast cancer.60

Similarly, age-related loss of NK function is implicated in the development of viral infections such as influenza, an annual killer of thousands of older adults.61 Studies show the importance of energetic NK cell function in producing vigorous responses to influenza and other vaccines.62 Immune senescence also reduces the numbers and changes the function of circulating T cells, shifting their population from a youthful one predominated by naïve T cells capable of recognizing and responding to new threats, towards an aging one predominated by memory T cells that have committed themselves to fighting just one specific type of insurgent.

Such a shift in T cell patterns makes us unnecessarily vulnerable, for example, to each season’s new influenza virus or emerging threats like West Nile virus, and at the same time less capable of responding to a host of vaccines.2,63

Inflammatory Cytokines

Inflammatory cytokines are signaling molecules that immune systems use to notify their various components of a need for attack, cleaning up an infection, and repair after tissue damage.64 Among the most prominent and potent inflammatory cytokines is interleukin-6 (IL-6).59

In youth, exquisite control systems regulate production of IL-6 and other cytokines to limit their actions only to active trouble sites, shutting down their production once a threat has been neutralized, and boosting production of other cytokines that contribute to resolution of inflammation (e.g., IL-10).59,64

But during immune senescence, these systems fail to operate properly, resulting in chronic elevations of IL-6, along with chronic suppression of anti-inflammatory cytokines.59,64 This state of immune senescence has been aptly referred to as “inflamm-aging.”59,64

Studies show that people who seem to be undergoing “healthy aging,” not succumbing to the inflammatory state, have lower levels of IL-6, and higher levels of anti-inflammatory cytokines, such as IL-10.59

Those with higher levels of IL-6 are much more likely to demonstrate frailty, which renders some older individuals especially vulnerable to falls, fractures, and infections.64

Immune senescence poses a major threat to longevity and quality of life by degrading three major defenses against outside attack or inside malignancies. Loss of bone marrow function, deleterious changes in circulating natural killer and T cells, and sharp increases in IL-6 and other inflammatory cytokines set one up for disability and death from infections, inflammation, and cancer.

Fortunately, breakthroughs in nutritional science now offer means of reversing immune senescence by providing a restructuring of the aging immune system’s three primary bulwarks: restoring bone marrow function, shifting circulating cell populations back towards a more youthful pattern, and reducing deadly elevations of IL-6.


A healthy thyroid gland not only acts as the body’s thermostat, but it’s also one of the major regulators of metabolism, including fat burning for energy.

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To order Triple Action Thyroid, call 1-800-544-4440 or visit www.LifeExtension.com

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**References**


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Contains milk.

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References

FLORASSIST® Throat Health
Item #01920 • 30 lozenges

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A culprit is an imbalance that involves a deficit of naïve T cells and a surplus of memory T cells. This produces a less vigilant immune response—or immune senescence, which has been linked to problematic outcomes in normal aging.

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<td><strong>Super Bio-Curcumin</strong> • 400 mg, 60 vegetarian capsules, Item #00407</td>
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<td>Super-absorbable formulation promotes healthy lipids, joint function, and DNA. Absorbs up to 7 times greater than conventional curcumin. Each bottle lasts two months.</td>
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<td><strong>AMPK Activator</strong> • 90 vegetarian capsules, Item #01907</td>
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<td>Activating AMPK “turns off” many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula (Gynostemma pentaphyllum and trans-tiliroside), promote AMPK activation.</td>
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<td><strong>Super Omega-3 EPA/DHA with Sesame Lignans &amp; Olive Extract</strong> • 120 softgels, Item #01982</td>
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<td>A highly refined fish oil blend derived from pristine waters off the coast of Alaska is formulated to remain exceptionally fresh. This purified EPA/DHA from Alaskan Pollock, plus sesame lignans and potent olive (fruit plus leaf) extract, provide essential components of the Mediterranean diet clearly differentiating this omega-3 formula from commercial fish oil.</td>
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<td><strong>Two-Per-Day</strong> • 120 tablets, Item #02015</td>
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<td>Compared to commercial multivitamin/multi-nutrient products like Centrum®, Two-Per-Day has up to 50 times the potency of specific nutrients, as well as unique ingredients. The newly formulated product now contains 5 MTHF, the biologically active form of folate, which is up to 7 times more bioavailable than folic acid. (Also available in capsule form at a slightly higher price.)</td>
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<td><strong>Health Booster</strong> • 60 softgels, Item #01989</td>
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<td><strong>FLORASSIST® Probiotic</strong> • 30 liquid vegetarian capsules, Item #01825</td>
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<td>Dual-encapsulation technology delivers potent doses of the six most important probiotic strains.</td>
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<td><strong>Super Ubiquinol CoQ10 with Enhanced Mitochondrial Support™</strong></td>
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<td>100 mg, 60 softgels, Item #01426</td>
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<td>The superior ubiquinol form of CoQ10 plus a natural compound (shilajit) shown to double mitochondrial CoQ10 levels.</td>
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<td><strong>Optimized Resveratrol with Nicotinamide Riboside</strong> • 30 vegetarian capsules, Item #02031</td>
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<td>High-potency vitamin D in a softgel to provide greater absorption into the bloodstream.</td>
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<td>Comprehensive support for an aging prostate gland utilizing standardized lignans, plus boron and phospholipids for enhanced absorption.</td>
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<td>Comprehensive formula providing 1,500 mcg of vitamin K1, 1,000 mcg of immediate-acting MK-4 vitamin K2, and 200 mcg of long-acting MK-7 vitamin K2 in a base of extra-virgin olive oil. This same vitamin K formulation is included in Health Booster.</td>
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<td>Promotes mitochondrial biogenesis (generation of new mitochondria) in aging cells.</td>
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<td>A hormone that declines with aging, benefits overall health.</td>
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<td>A highly concentrated 98% polyphenol extract delivering 45% of the health-promoting catechin EGCG.</td>
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<td><strong>Life Extension Mix™ • 315 tablets, Item #02055</strong></td>
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<td>This upgraded high-potency multi-nutrient formula contains 5-methyltetrahydrofolate (5-MTHF), the biologically active form of folate that is up to 7 times more bioavailable than folic acid.</td>
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<td><strong>Bone Restore • 120 capsules, Item #01726</strong></td>
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<td>Highly absorbable forms of calcium and FruiteX B® OsteoBoron®, magnesium, zinc, and vitamin D3. Also available with vitamin K2 at a slightly higher price. (Those taking Super K or Health Booster don’t need additional vitamin K.)</td>
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<td><strong>Cognitex® with Brain Shield® • 90 softgels, Item #01896</strong></td>
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<td>Optimal support for the brain. Includes gastrodin, alpha-glyceryl phosphoryl choline, vinpocetine, phosphatidylserine, uridine-5'-monophosphate, and more. Available with or without pregnenolone.</td>
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<td><strong>Enhanced Super Digestive Enzymes with Probiotics • 60 vegetarian capsules, Item #02022</strong></td>
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<td>Contains amylase, protease, lipase, cellulase, and lactase to break down protein, starch and short sugar chains, fat, cellulose, and lactose. It has the added benefit of the probiotic Bacillus coagulans, which creates a coating that resists digestion in the stomach, allowing it to fully colonize in the intestines.</td>
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<td><strong>Immune Senescence Protection Formula™ • 60 vegetarian tablets, Item #02005</strong></td>
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<td>Standardized full-spectrum Reishi mushroom extract with Cistanche and Pu-erh tea extracts to help restore youthful immune balance.</td>
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<td><strong>Triple Action Thyroid • 60 vegetarian capsules, Item #02003</strong></td>
<td>$36</td>
<td>$21.60 (four-bottle purchase)</td>
</tr>
<tr>
<td>A combination of ashwagandha, guggul, and Korean ginseng extract work in synergy to combat many of the ailments arising from a poorly functioning, suboptimal thyroid.</td>
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</tr>
<tr>
<td><strong>European Milk Thistle • 60 softgels, Item #01822</strong></td>
<td>$28</td>
<td>$16.88 (four-bottle purchase)</td>
</tr>
<tr>
<td>High-absorption phospholipid-enhanced formula delivers nearly 5 times more active components to the bloodstream to support detoxification processes as well as promote liver health and function.</td>
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<tr>
<td><strong>Skin Restoring Phytoceramides • 350 mg, 30 vegetarian capsules, Item #01596</strong></td>
<td>$25</td>
<td>$15.53 (four-bottle purchase)</td>
</tr>
<tr>
<td>Oral phytoceramides derived from wheat can reach the skin’s deepest layers to offset the body’s natural decline with age.</td>
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<tr>
<td><strong>ArthroMax® Advanced with UC-II® and AprèsFlex® • 60 capsules, Item #01618</strong></td>
<td>$36</td>
<td>$21.60 (four-bottle purchase)</td>
</tr>
<tr>
<td>Promotes joint health and may promote comfortable joint structure and function.</td>
<td></td>
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</tr>
<tr>
<td><strong>FLORASSIST® Oral Hygiene • 30 lozenges, Item #02011</strong></td>
<td>$20</td>
<td>$12.15 (four-bottle purchase)</td>
</tr>
<tr>
<td>This unique blend of two powerful, oral probiotics—S. salivarius and Bacillus coagulans—inhbits harmful bacteria that develop in your mouth, affecting your teeth, gums, and overall health.</td>
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<tr>
<td><strong>Advanced Bio-Curcumin® with Ginger and Tumerones • 30 softgels, Item #01808</strong></td>
<td>$30</td>
<td>$18.23 (four-bottle purchase)</td>
</tr>
<tr>
<td>Triple-action formula acting on multiple signaling pathways to deliver broad-spectrum protection against inflammation.</td>
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</tr>
<tr>
<td><strong>Neuro-Mag® Magnesium L-Threonate • 90 vegetarian capsules, Item #01603</strong></td>
<td>$40</td>
<td>$24.30 (four-bottle purchase)</td>
</tr>
<tr>
<td>Optimal form of magnesium to protect synaptic density of neurons.</td>
<td></td>
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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
In response to medical reports that are misinterpreted by the media, Life Extension® has historically issued point-by-point rebuttals when the study’s methodologies/analyses are scientifically flawed and/or the findings blatantly false.

In response to sensationalized headlines appearing earlier this year about a flawed vitamin D study, Life Extension reached out to a medical doctor who has been fighting the establishment almost as long as we have.

Before you read Dr. Dean’s detailed rebuttal to this study published by the American Medical Association, it’s important for you to know why these kinds of reports garner so much media attention.

In pharmaceutical corporate boardrooms, charts are routinely presented showing how many people are projected to contract a terrible disease. Data about the potential benefits of a patented drug follows the chart projection. Then a financial calculation is done to show how much money will be made if the pharmaceutical company pushes this drug through the FDA’s arduous approval process.

An uncertainty has arisen regarding the lucrative financial projections coveted by drug companies. What if the chart showing growing numbers of aging Americans contracting a degenerative disease goes the other way…in other words declines? This destroys the profit expectation and incentive to spend hundreds of millions if not billions on new drug candidates.

The greatest threat to the profitability of Big Pharma may be vitamin D. This vitamin costs virtually nothing and has an incredible amount of data showing its ability to decimate the financial projections of drug companies who look forward to lots of aging Americans being diagnosed with some form of cancer every year. (Refer to chart on this page.)

Drug company ads dominate media advertising the way tobacco ads did in the 1950s through 1960s. It is in the economic interests of Big Pharma for the media to air headlines warning Americans to avoid vitamin D (and other supplements). The more people who believe these flawed reports, the more money the pharmaceutical industry makes.

As you will read, not only is this analysis attacking vitamin D without scientific merit, but newly published data reveals vitamin D to be even more effective in preventing death and disability than previously known. Drug companies would prefer that you not read these reports on vitamin D.
“Vitamin D Ineffective for Hypertension”

On March 15, 2015, the journal JAMA Internal Medicine published a systematic review and meta-analysis titled “Effect of Vitamin D Supplementation on Blood Pressure.”1

The authors of the article stated that their purpose was to conduct a systematic review of clinical trials to evaluate whether vitamin D supplementation reduces blood pressure compared to placebo. In their meta-analysis, they included studies that reported any baseline 25-hydroxyvitamin D blood levels, any blood pressure levels, studies that lasted as little as four weeks, and which involved supplementation with a variety of forms of vitamin D, including vitamin D2, vitamin D3, calcitriol (1,25-hydroxyvitamin D3), and 1-alpha-hydroxylated versions of vitamin D (paricalcitol and doxercalciferol). The primary results the authors were looking for were changes in office-measured systolic or diastolic blood pressure readings.

The meta-analysis included 46 trials involving a total of 4,541 participants. After analyzing participant data, the authors proclaimed, “Vitamin D supplementation is ineffective as an agent for lowering blood pressure, and thus should not be used as an antihypertensive agent.”

Two days later, on March 17th, CBS News jumped on the bandwagon and trumpeted, “Vitamin D useless for lowering blood pressure.”2 CBS News medical contributor Dr. David Angus stated that although vitamin D was “the second most prescribed or taken vitamin in the country, there is no benefit that anybody derives… it doesn’t work in anybody,” and cautioned that “it may cause significant harm.” Dr. Angus went on to allege that “too much vitamin D in the blood can be harmful, causing nausea, constipation, and even damage to the kidneys.”
I was surprised at the conclusions reached by the *JAMA Internal Medicine* article, and even more dismayed by the off-the-wall “analysis” by CBS News. I knew of the multiple benefits of higher doses and increased blood levels of vitamin D, as well as the dangers to health of low levels, and that lower blood levels of vitamin D are associated with higher blood pressure levels in cross-sectional studies, and with increased rates of hypertension.

Nevertheless, the above-cited meta-analysis on the surface sounded pretty definitive—followed by the drubbing from the CBS News medical commentator. A rational person would assume that the studies involved in the meta-analysis were studies of hypertensive patients who had deficient or low levels of vitamin D, and who were treated with therapeutic doses of vitamin D or placebo for an adequate period of time.

However, when I examined the individual studies that comprised the meta-analysis, a different picture emerged. Very few of the studies met these presumptive criteria. What I found was a mishmash of studies that used varying doses of vitamin D, ranging from 30 IU to 7,000 IU per day (including several studies which used doses as high as 300,000 IU, given as a single injectable dose administered to subjects who were, for the most part, neither hypertensive nor deficient in vitamin D).

Like many long-time readers of *Life Extension*, I believe that an optimal blood level of vitamin D should be higher than 50 ng/mL, and for most people to attain this level, it is necessary to consume between 5,000 to 10,000 IU per day.

Vitamin D blood levels were considered by the “meta-analyzers” to be “deficient” if less than 10 ng/mL, “insufficient” (10-20 ng/mL), and “adequate” (greater than 20 ng/mL). In contrast, Life Extension’s recommended optimal blood level for vitamin D is 2.5 times higher than the blood level considered adequate by the meta-analysis authors.

### Study Design and Details

The analysis included 46 studies. Of these, only 16 of the studies included participants who had mean systolic blood pressure greater than 140 mmHg (1,361 subjects), while 30 of the studies’ participants had mean systolic blood pressure less than 140 mmHg (3,180 subjects). Thus, nearly 75% of the participants in the study were not hypertensive. It is not surprising that vitamin D in any amount had little or no effect on those with normal blood pressure—in fact, it is reassuring that vitamin D does not further lower blood pressure in normotensives. A potential problem with most antihypertensive drugs is that too high a dose can cause dangerously low blood pressure—whether one is hypertensive or not. Correcting a nutritional deficiency should not be expected to lower normal blood pressure.

### Inappropriate Study Selection

It became increasingly clear that the problem with this meta-analysis was the selection of the studies on which the analysis was based. Few of the studies directly addressed the key question the meta-analysis was designed to answer: i.e., does supplemental vitamin D have a positive effect on hypertensive subjects with low levels of vitamin D? Few of the studies specifically included hypertensive subjects or subjects who suffered from vitamin D deficiency (or insufficiency). In fact, many of the studies included only “healthy” subjects, and several specifically excluded those who were hypertensive. In addition, there was no standard form of vitamin D or range of vitamin D used.

As mentioned previously, forms of vitamin D included vitamin D2 (ergocalciferol), vitamin D3 (cholecalciferol), calcitriol (1,25-hydroxyvitamin D3), paricalcitol, and doxercalciferol. Length of the studies varied from as short as four weeks to as long as 18 months. Most significant was the fact that only a few of the studies actually used blood pressure as a major end-point of the study. Most were primarily concerned with other parameters, and considered blood pressure as a secondary or incidental event.
Another study reported no benefit from vitamin D supplementation in depressed people with low levels of serum vitamin D, to whom 40,000 IU of vitamin D3 were administered each week for six months. This study specifically excluded subjects with hypertension from the trial.12

Another shortcoming in many of the trials was the limited length of the trial itself. For example, one study tested the effect of a single oral dose of 100,000 IU vitamin D3 on patients with peripheral arterial disease (PAD), and hoped for positive changes after only one month!13 PAD does not come on overnight—and is not likely to be reversed in one month with a single dose of anything.

Another study involved healthy (not hypertensive) subjects, with vitamin D levels that were either normal or not checked. Subjects in this study were given 200,000 IU of vitamin D3 per month for two months, followed by 100,000 IU per month for the next sixteen months. Not surprisingly, the authors found that vitamin D supplementation “had no effect on systolic or diastolic blood pressure in predominantly white, healthy adults without severe vitamin D deficiency.”10

Of all the studies in the meta-analysis, the study that administered the highest dose of vitamin D3 (300,000 IU via intramuscular injection) specifically excluded subjects with known clinical deficiency of vitamin D.11

Consequently, the 46 papers that were included in the meta-analysis were a poorly selected mélange of studies investigating a hodge-podge of unrelated physiological phenomena. The only unifying characteristics seemed to be that some dose of some form of vitamin D was used to evaluate some physiological functions that happened to include a measurement of blood pressure.

For example, one of the studies evaluated the effects of small doses of vitamin D3 (0, 200, 400, or 600 IU) in healthy (i.e., not hypertensive nor D-deficient) young (20-40) and older (over 64) men and women. Not surprisingly, the researchers found no significant effects of vitamin D on cardiovascular risk factors. What did they expect from these normal volunteers? The researchers conceded: “Putative effects of vitamin D on cardio-metabolic health will only be evident at higher intakes than the current RDA.”

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Another trial studied the effect of high-dose vitamin D3 (50,000 IU per week) for six months in patients suffering from heart failure.14 Over 60% of the subjects were classified as NYHA Class II, which means that the patients had cardiac disease resulting in slight limitation of physical activity, were comfortable at rest, but ordinary physical activity resulted in fatigue, palpitation, shortness of breath (dyspnea), or anginal pain. The remaining patients (36%) were in Class III, which means that they had severe cardiac disease with marked limitation of physical activity. Less-than-ordinary activity caused fatigue, palpitation, dyspnea, or angina. These were all very sick people, suffering from a serious chronic disease. Again, it is not surprising that increasing their vitamin D levels—even for six months—did not reverse their condition.
It is obvious that the articles selected for this meta-analysis were all over the map. It was a collection of miscellaneous studies grouped together and “analyzed” to produce what appeared to be a previously determined outcome—i.e., that vitamin D was not an effective treatment for hypertension for anyone—even though that premise was not the focus of the majority of studies included in the meta-analysis. This reminded me of the old computer dogma, GIGO—garbage in, garbage out.

Positive Results Nonetheless

Despite the pattern of inappropriate study selection for this analysis, a number of the studies reported positive results.

In one study, 34 type II diabetics with low serum vitamin D levels (less than 20 ng/mL), were given 100,000 IU of vitamin D2 (ergocalciferol) or placebo, and monitored for eight weeks. Vitamin D2 “significantly decreased systolic blood pressure by 14 mmHg.”15

One of the earliest studies in the meta-analysis used daily doses of 1 mcg of alfalcaldol (a synthetic vitamin D analog, roughly equivalent to 40 IU of vitamin D3) in 29 hypocalcemic patients. After six months, the authors reported a significant reduction of both systolic and diastolic blood pressures, compared with placebo. They concluded that a physiologic amount of active vitamin D has hypotensive effects and can be beneficial for patients with high blood pressure.16

In another study by the same team, 33 patients with primary hyperparathyroidism, mild hypercalcemia, and elevated diastolic blood pressure were given 1 mcg of alfalcaldol or placebo for six months. The scientists found a significant reduction of diastolic blood pressure, and concluded: “Vitamin D can lower blood pressure in hypercalcemic patients.”17

In yet another study, 148 women with vitamin D insufficiency (25OHD less than 20 ng/mL) received daily doses of either 800 IU vitamin D3 plus 1,200 mg of calcium or 1,200 mg of calcium for eight weeks. The results showed that 81% of the subjects in the vitamin D3 plus calcium group compared with only 47% in the calcium group showed a decrease in systolic blood pressure (SBP) of 5 mmHg or more. The scientists concluded that “short-term supplementation with vitamin D3 and calcium is more effective in reducing SBP than calcium alone.”18

Paradoxically, the senior author of the meta-analysis (which claimed that vitamin D was ineffective as an antihypertensive agent) authored an earlier paper, in which he demonstrated that single doses of 100,000 or 200,000 IU of vitamin D3 administered to 39 diabetics with 25OHD levels less than 40 ng/mL resulted in significant lowering of systolic blood pressure after eight weeks, causing him to conclude that “high-dose vitamin D3 improved systolic blood pressure... in patients with type II diabetes.”19

African-Americans are known to have significantly higher rates of hypertension than whites. Scientists from Brigham and Women’s Hospital, Boston, conducted a double blind study of 283 African Americans, using doses of vitamin D3 as high as 4,000 IU a day, which resulted in significantly lowered systolic pressure.20

Scientists from the University of Verona, Verona, Italy, administered 4,000 IU of vitamin D3 per day to 13 of 23 patients who suffered from chronic heart failure. The patients’ mean age was 74, and all had vitamin D
levels less than 30 ng/mL. After six months, systolic blood pressure was lower in those treated with D3, and ejection fraction was improved.21

**Other Studies (Not Included in Meta-Analysis)**

In 2009, German scientists investigated the effect of vitamin D (calcitriol—the active form of vitamin D) levels on mortality in a cohort of 510 patients with serious, life-threatening illnesses: 67.7% with heart failure (two-thirds in end stage), 64.3% with hypertension, 33.7% with coronary heart disease, 20.2% with diabetes, and 17.3% with renal failure.

Many of these patients had multiple co-morbidities. The scientists assessed vitamin D (calcitriol) status at the beginning of the study, and assigned the patients to the following quintiles: <16.7 ng/L, 16.7-25.2 ng/L, 25.3-33.2 ng/L, 33.3-43.4 ng/L, and >43.4 ng/L.

No supplementation was provided, although the patients were administered standard medications, and were followed for one year.

Broken down by quintiles, the probability of survival was: 66.7% in the lowest quintile, 82.2% in the second quintile, 86.7% in the third quintile, 88.8% in the fourth quintile, and 96.1% in the highest quintile. (See Figure 1.) These survival improvement percentages in those with higher vitamin D blood levels are nothing short of astounding.

Significantly, none of the patients with calcitriol concentrations >58.5 ng/L died during follow-up.22

More recently, in 2013, scientists from Johns Hopkins University, Baltimore, MD, examined 10,170 participants using National Health and Nutrition Examination Survey data to estimate hazard ratios (HRs) for all-cause and cardiovascular disease mortality for each 10-unit increase in serum 25OHD. The authors concluded that there is “an inverse association between 25OHD and all-cause and cardiovascular disease mortality in healthy adults with serum 25OHD levels of <21 ng/mL.” Said differently, 25-hydroxyvitamin D blood levels below 21 ng/mL in this study increased the risk of dropping dead! (See Figure 2)23

**Why Interventionist Vitamin D Meta-Analyses Appear to Fail**

This pattern of arriving at erroneous conclusions about vitamin D from an analysis of inappropriately selected studies has happened before. For example, a recent paper reported the positive effects of high-dose (300,000 IU over eight weeks) vitamin D2 (ergocalciferol) on vascular endothelial function and flow mediated dilation.24

The authors conceded that only three other studies had arrived at a similar (positive) conclusion15,25,26 while the rest failed to find any benefit. The authors explained, “The studies where vitamin D therapy was unable to show improvement often used low-dose vitamin D supplementation...” and “…vitamin D was supplemented even when the baseline levels [of vitamin D]
were within normal limits.” A third major reason may have been that flow mediated dilation or endothelial function (like blood pressure) was not abnormal.

While reviewing papers in the meta-analysis, I encountered another recently published article that was also not included in the meta-analysis. Appearing in the journal Blood Pressure Monitoring, it was titled "The Effect of Vitamin D Supplementation on Blood Pressure in Patients with Elevated Blood Pressure and Vitamin D Deficiency." This was exactly the type of study that should have been the prototype for the meta-analysis. This was a straightforward double-blind placebo-controlled study of 42 patients with elevated blood pressure who suffered from vitamin D deficiency (defined by authors as serum 25-hydroxyvitamin D levels less than 30 ng/ml). Half of the subjects were treated with 50,000 IU vitamin D3 each week for eight weeks, while the other half were given an identical-appearing placebo. Both groups continued their use of conventional antihypertensive medications.

The findings of the study showed a significant reduction in systolic, diastolic, and mean arterial pressure in those in the vitamin D group. Despite improved blood pressure, 42% of the vitamin D group still had systolic blood pressure in excess of 140 mmHg, and 68% had diastolic blood pressure over 90 mmHg. However, 95% (i.e., twice as many) of those in the placebo group (whose blood pressure did not change) remained over 140/90.

This study shows that while vitamin D supplementation reduces blood pressure readings, hypertensives often need additional support to achieve optimal readings, which are considered to be in the range of 115/75 for most individuals.

Summary

Rather than being a meta-analysis of relevant studies of the effect of therapeutic doses of vitamin D or placebo on vitamin D-deficient hypertensive patients, the JAMA Internal Medicine article was a selection of unrelated, often irrelevant studies, which appeared to indicate that vitamin D had no effect on blood pressure.

However, the authors were often not just comparing apples to oranges—they were comparing apples and oranges to the whole fruit basket!

What the meta-analysis did show was that high-dose vitamin D will not lower normal blood pressure, nor affect blood pressure of hypertensives with normal serum vitamin D. Furthermore, if one “reads between the lines,” and analyzes the studies that were relevant, it becomes clear that vitamin D appears to be a useful adjunct to help normalize blood pressure in vitamin D-deficient hypertensives.

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

Editor’s Note: People take vitamin D supplements for a variety of reasons including reduced risks of certain cancers and suppression of chronic inflammation. Published reports over the past 10 years indicate that higher vitamin D levels may help protect against virtually all degenerative diseases.

Hypertension, however, has not been a primary reason people supplement with vitamin D as it does not reduce blood pressure enough in most individuals to achieve optimal ranges.

Optimal blood pressure readings for most people are about 115/75 mmHg.

Life Extension’s recommended anti-hypertensive drug is a generic called telmisartan taken in the dose of 40 to 120 mg once daily. In addition to lowering blood pressure, telmisartan improves markers of endothelial function and has demonstrated some impressive longevity benefits.

The next article reports on remarkable new studies showing huge improvements in ischemic stroke outcomes in those with higher vitamin D blood levels.

**References**


WHY ISN'T EVERYONE SUPPLEMENTING WITH VITAMIN D?
Popular multivitamin supplements still don’t provide enough vitamin D to yield optimal health benefits. Most commercial multivitamins contain 400 to 600 IU of vitamin D, a potency that provides little real-world benefit.

With evidence showing reduced mortality in those with higher vitamin D blood levels, an urgent need exists to alert the public about the importance of taking the proper dose of this low-cost vitamin. Failure to properly supplement contributes to a host of premature illnesses along with increased national health care costs.

Compelling research has demonstrated that vitamin D blood levels in the range of 50 to 80 ng/mL are associated with reduced mortality and a lower risk of common diseases.\(^1\,^2\)

A considerable volume of published literature documents a connection of insufficient or deficient 25-hydroxyvitamin D blood levels\(^3\) with higher risks of cancer,\(^4\)-\(^6\) vascular disease,\(^7\)-\(^10\) and chronic inflammation.\(^11\)-\(^13\)

Low vitamin D status has long been associated with loss of bone density. This limited view of vitamin D’s biological effects is still taught in many medical textbooks, leading some doctors to view vitamin D only for its value in reducing osteoporosis risk.

Yet vitamin D has clinical applications for a vast array of health conditions. This article reviews some recent findings that reveal an even wider range of protective benefits conferred by this readily available dietary supplement.
Post Stroke Functional Outcome

Stroke is the leading cause of serious long-term disability. An estimated 6.8 million Americans (2.8% of the entire adult population) are living after having had a stroke. When a stroke occurs, 40% of its victims experience moderate to severe debilitation requiring special care, and 15% die shortly thereafter.

Vitamin D deficiency is pervasive among stroke victims, and those with the lowest levels of vitamin D have been shown to have the poorest functional outcomes. In fact, a recent study showed that for each 10 ng/mL decrement in vitamin D, the odds of a poor 90-day post stroke functional outcome doubled.

To put this in perspective, those who don’t supplement with high doses of vitamin D typically have 25-hydroxyvitamin D levels under 20 ng/mL. Those who properly supplement should strive to obtain levels of 25-hydroxyvitamin D over 50 ng/mL. Based on this study’s findings, people with these higher vitamin D levels would be far more likely to avoid permanent institutional confinement if they suffered an ischemic stroke.

Another recent study involving 818 stroke patients showed very similar results. Those with an adequate vitamin D level of 30 ng/mL or above showed a 90% better improvement in functional outcomes compared to those who were severely deficient (<10 ng/mL).

Experts believe that in order to prevent many of the age-related diseases, people should maintain a vitamin D blood level between 50 to 80 ng/mL.
These stroke studies are showing robust improvement in functional outcome with just a **sufficient** vitamin D blood level. Based on the number of studies showing vascular protective benefits of vitamin D, those who maintain optimal vitamin D levels, along with comprehensive **blood testing** to correct other risk factors, will likely decrease their stroke risk and reduce the odds of permanent disability in the event one of their cerebral arteries becomes occluded (ischemic stroke).^{29}

### Support for Diabetics

**Beta cells** are insulin-producing cells in the pancreas. When the beta cells die, people become insulin-dependent diabetics. Without insulin, there is nothing to deliver glucose into cells for energy production. This leads to high circulating glucose blood levels that contribute to a long list of deadly disorders that include heart disease,^{30} Alzheimer’s,^{31} and cancer.^{32}

Vitamin D has been documented to prevent high glucose-induced beta cell apoptosis (death). This is because beta cells contain active receptors for vitamin D, just like every other cell in the body.^{33-35}

### A Link between Vitamin D and Multiple Sclerosis

It is well known that there are higher rates of vitamin D deficiency in **colder climates** of the world due to the lack of sun. This has caused a greater chance of having an immune system-related illness.

**Multiple sclerosis** (MS) is an autoimmune disease caused when the body’s own T lymphocytes, B lymphocytes, and macrophages attack the **myelin sheath** of neurons.^{36} Those living in the northern part of the United States are twice as likely to develop multiple sclerosis, and those in Canada have a **5-times** greater risk compared to people residing in the southern US. This geographical data, along with a multitude of studies that explain the mechanisms and causation, has led many researchers to believe that MS is heavily influenced by vitamin D deficiency.^{37}

A study published by *PLOS Medicine* identified single nucleotide polymorphisms that were strongly associated with lower **25-hydroxyvitamin D** levels.^{38} The researchers studied the odds of MS on those with genetically lower vitamin D levels from the International Multiple Sclerosis Consortium study. Considered the largest genetic association study to date for MS, it included **14,498** subjects with MS and **24,091** healthy controls. The authors concluded that genetically lowered vitamin D levels were strongly associated with an increased risk for MS.^{38}
This new data heavily reinforces the statistics and research on vitamin D for MS. Trials show that more than 90% of people with MS have deficient vitamin D. Deficient is defined at a level below 20 ng/mL. Vitamin D can even mediate the direct effects of the immune cells that attack the myelin sheath, a hallmark pathological mechanism of MS. When these aggressive immune cells were extracted from MS patients and exposed to vitamin D, their division was slowed. This signifies the imposing control vitamin D can have on autoimmune diseases such as MS.

Vitamin D Lowers Inflammatory Biomarkers

Interleukin-6 (IL-6) is an inflammatory cytokine. At high levels, this cytokine has been linked with several types of cancers. Overweight individuals have much higher rates of inflammatory cytokines like interleukin-6.

A compelling study documented marked reductions of interleukin-6 when vitamin D is combined with weight loss. The study involved 218 overweight postmenopausal women who were divided into two groups. Both groups had weight loss interventions, but one group was given 2,000 IU per day of oral vitamin D3. Both groups achieved a 5% to 10% weight loss, but the group that received the vitamin D supplement showed an impressive 37.3% reduction in interleukin-6 levels compared to the placebo which only had a 17.2% reduction.

Psychiatric Disorders

Interesting research is showing higher levels of vitamin D play an important role during pregnancy for preventing many different psychiatric disorders. The vitamin D receptor emerges in the brain stem through the embryonic development of rats. This indicates and reinforces the idea that vitamin D is important for gestational development. Additional studies have shown that vitamin D deficiency in the mother can lead to impaired growth of the fetus.

Attention Deficit Hyperactive Disorder (ADHD)

A fascinating study analyzing vitamin D blood levels in 1,650 mothers showed that for each 10 ng/mL increment in vitamin D levels, their children had 11% less ADHD-like symptoms. This type of research has heavily influenced the demand for prenatal vitamins. However, most multivitamins only contain a fraction of the vitamin D that is needed to be therapeutic. The trivial amount of vitamin D in most prenatal vitamins is not enough to raise a vitamin D level by 10 ng/mL.

Schizophrenia

An imbalance of dopamine has been hypothesized to be a cause of schizophrenia. The vitamin D receptor emerges in the brain stem at the same time as the peak period of dopamine cell birth in rat embryos.
There has been a high correlation between vitamin D deficiency and schizophrenia. The correlation has influenced a study to show if vitamin D deficiency was prevalent in those having an acute episode.

The study subjects were divided into three groups: 40 patients who were reported to be having an acute episode, 41 patients in remission, and 40 healthy controls.

Those who reported to be having an onset of schizophrenic episodes had far lower levels of vitamin D compared to schizophrenics in remission. The healthy controls had the highest levels of vitamin D.

**Ignored Age-Related Panacea**

Life Extension® has been writing about the health benefits of vitamin D for many decades. Fortunately, researchers are finally catching up with these findings and devoting resources to discovering and documenting new applications of vitamin D. What might be surprising is that the new research discussed in this article was released just within this last year.

There is an immense archive of literature documenting the health benefits of this single vitamin. Every day, more research findings are being published. In fact, by the time this article is published, there will be even more noteworthy studies released.

Current medical teachings need to be updated to include evidence that vitamin D provides support not just bone health, but also to reducing all-cause mortality through its system-wide benefits. Vitamin D is the only vitamin that has receptors for it located on every cell. With the cumulative and consistent evidence backing its efficacy, this vitamin should be an essential part of everyone’s daily health regimen.

The cost of conventional treatment for age-related diseases is staggering and Medicare is on the hook for a huge unfunded liability.

People today have an unprecedented opportunity to reduce their risk of needing conventional treatment using a low-cost vitamin supplement. The typical dose range is 5,000 to 8,000 IU of vitamin D daily taken with a meal for better absorption.

Annual blood tests can enable one to know if they are taking the proper dose of vitamin D they need to achieve optimal levels of 25-hydroxyvitamin D.

**Summary**

While the use of vitamin D has increased dramatically, levels in common commercial multivitamins (400 to 600 IUs) are still far too low to provide real-world benefits.

Extensive research has demonstrated that higher vitamin D blood levels are associated with reduced mortality risk and specific diseases such as diabetes, stroke, and multiple sclerosis, along with other autoimmune diseases and psychological disorders.

Vitamin D dosing in the range of 5,000 to 8,000 IU each day should be taken with a meal for better absorption.

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

**References**

WHY ISN'T EVERYONE SUPPLEMENTING WITH VITAMIN D?

Ultra Natural Prostate formula provides the latest scientifically validated botanical extracts shown to promote healthy prostate function. No other prostate protection formula provides such a broad array of nutrients to support the multiple factors involved in the health of the aging prostate gland. Ultra Natural Prostate contains:

- **Standardized lignans** provide support for prostate cells against excess estrogen levels.1,3
- **AprèsFlex®** supports normal inhibition of 5-lipoxygenase or 5-LOX, an enzyme associated with undesirable cell division changes.5,6
- **Stinging and Dwarf nettle root extracts** help support prostate cells against excess estrogen levels.6,7
- **Saw Palmetto CO extract** helps inhibit dihydrotestosterone (DHT) activity in the prostate, helps support normal urinary flow, and helps regulate inflammatory reactions in the prostate.8,11
- **Pygeum extract** helps suppress prostaglandin production in the prostate and supports healthy urinary patterns.2,13
- **Pumpkin seed oil**, enhances the composition of free fatty acids and augments saw palmetto’s benefits.1-3
- **Beta-sitosterol** helps maintain healthy DNA structure.24-26
- **Graminex® Flower Pollen Extract™**, has been shown to help relax the smooth muscles of the urethra and help regulate inflammatory reactions.22,26
- **Boron** has been shown to slow elevation of prostate-specific antigen (PSA).25-27
- **Lycopene** supports efficient cellular communication, helps maintain healthy DNA, regulates hormonal metabolism, and promotes healthy prostate size and structure.26-32
- **Phospholipids** enhance absorption of active compounds.

**References**

20. Available at: http://www.med.nyu.edu/content/chi/chi.asp?

**To order Ultra Natural Prostate, 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.
Despite a healthy diet and exercise, aging individuals often find themselves under assault from rising blood sugar levels due to a multitude of factors such as:

- Excess gluconeogenesis, (glucose produced in the liver from protein)¹
- Rapid conversion of any starch—including whole grains—into glucose²

An all-natural, multi-pronged approach has been designed to support the natural balance of key glucose pathways!

Tri Sugar Shield® is designed to support healthy glucose metabolism in aging individuals within the normal range.

**TRI SUGAR SHIELD® THREE ACTIVE NUTRIENTS**

**Sorghum Extract**

Sorghum helps maintain healthy blood sugar levels among those in normal range by:

- Balancing the rate of sugar manufacture in the liver³
- Promoting insulin sensitivity⁴
- Regulating PPAR-gamma, a metabolic thermostat that controls glucose metabolism⁵,⁶
- Regulating alpha-amylase, which controls the release of sugar from starch⁶

**Mulberry Leaf Extract**

Mulberry leaf extract targets two different mechanisms by:

- Supporting glucose transporter GLUT⁴ that moves glucose out of the bloodstream and into muscle and liver cells⁶
- Promoting insulin sensitivity⁹

**Phloridzin**

Phloridzin helps maintain healthy blood sugar levels among those in the normal range by:

- Regulating carrier protein SGLT¹, helping to block absorption of glucose into the bloodstream⁶
- Regulating carrier protein SGLT², in turn supporting glucose elimination via urine¹¹

By targeting all of these diverse glucose pathways, Tri Sugar Shield® delivers broad-spectrum support to help naturally stabilize already healthy glucose levels!

Supports Healthy Blood Glucose Levels

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
New research on the vital benefits of vitamin D emerges on a daily basis. Studies confirm that optimal levels of vitamin D are in the range of 50-80 ng/mL of 25-hydroxy vitamin D. Life Extension® has created a large selection of highly absorbable vitamin D supplements in softgels to help you to achieve your individual vitamin D goals. Keep in mind that you may already be getting 1,000-3,000 IU of vitamin D in your current multi-nutrient formulas.

**Vitamin D3 • 1,000 IU**
250 softgels • Retail: $12.50
Super Sale Four bottles: $7.60 ea.
For most people, a 1,000 IU potency is insufficient to attain optimal vitamin D blood levels. However, this potency may be suitable for smaller individuals who obtain 2,000-3,000 IU in their multi-nutrient formulas (and children). Item # 01751

**Vitamin D3 • 5,000 IU With Sea-Iodine™**
60 capsules (non-softgel) • Retail: $14
Super Sale Four bottles: $8.44 ea.
Most people, especially those seeking to reduce their salt intake, do not ingest enough iodine. Combining 5,000 IU of vitamin D3 with 1,000 mcg of iodine into one capsule makes taking these two nutrients economical and convenient. Item # 01758

**Vitamin D3 • 2,000 IU (Natural Mint Flavor)**
1 ounce • Retail: $28
Super Sale Four bottles: $16.88 ea.
Great for travel and for those individuals who have difficulty absorbing enough vitamin D3 from softgels, this liquid vitamin D is ideal. Item # 01732
Also available without mint. (Item # 00864)

**Vitamin D3 Liquid • 2,000 IU**
2,000 IU
1 ounce • Retail: $28
Super Sale Four bottles: $16.88 ea.
Great for travel and for those individuals who have difficulty absorbing enough vitamin D3 from softgels, this liquid vitamin D is ideal. Item # 01732
Also available without mint. (Item # 00864)

**Vitamin D3 • 7,000 IU**
60 softgels • Retail: $14
Super Sale Four bottles: $8.51 ea.
For those already obtaining 1,000-3,000 IU of vitamin D in their multi-nutrient formulas, this 7,000 IU potency is what may be needed to achieve optimal blood levels. Item # 01713

**Vitamin D3 Liquid • 5,000 IU**
1,000 IU
1 ounce • Retail: $28
Super Sale Four bottles: $16.88 ea.
Great for travel and for those individuals who have difficulty absorbing enough vitamin D3 from softgels, this liquid vitamin D is ideal. Item # 01732
Also available without mint. (Item # 00864)

To order any of these high-potency vitamin D3 supplements, call 1-800-544-4440 or visit www.LifeExtension.com

Caution: Individuals consuming more than 2,000 IU/day of vitamin D (from diet and supplement(s) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10,000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.

*If you have a thyroid condition or are taking antithyroid medications, do not use without consulting your healthcare practitioner.

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.
Innovative FIBER Improves METABOLIC HEALTH

After-meal elevations in blood sugar concentrations are a significant risk factor for the development of diabetes, cardiovascular disease, and certain cancers. Post-meal glucose spikes are also linked to Alzheimer’s disease, kidney failure, and retinal damage. Ingestion of simple sugars and starchy foods are primary causes of these postprandial glucose changes.

The good news is that researchers have identified a unique fiber called alpha-cyclodextrin that significantly reduces deadly glucose surges. For 30 years, Japanese researchers have investigated another benefit of alpha-cyclodextrin. What they discovered is that this compound also selectively absorbs and eliminates bad fats, such as trans fats and saturated fats, before reaching the bloodstream, while sparing good fats, such as omega-3s, to deliver their benefits. Not only does this “fat reduction” reduce calories absorbed, it also reduces the harmful effects of “bad” fats along with cholesterol levels in the bloodstream.

Together, the ability of this innovative fiber to remove harmful fats from the bloodstream and reduce dangerous after-meal blood sugar spikes makes it an important addition for anyone who wishes to improve their metabolic health and reduce their risk of a wide spectrum of deadly diseases.
The study found that alpha-cyclodextrin reduced the glycemic response to standard carbohydrate meals and may be useful for reducing the glycemic response to carbohydrates. But preventing glucose spikes forms just one part of the overall, longer-term benefits of alpha-cyclodextrin.

**A Unique and Safe Fat Blocker**

Ingestion of too many carbohydrates, with the following postprandial blood sugar spikes that result, is just one dietary contributor to obesity and chronic disease. Equally as dangerous to one’s health and longevity is the presence of “bad” fats in the bloodstream. Excess saturated fat in the diet is a leading cause of lipid disturbances, an ongoing epidemic of obesity, and the resulting high incidence of cardiovascular disease. Even with the most dedicated commitment to limit unhealthy fats, many individuals find it difficult to balance their blood lipid profiles, lose weight, and reduce their risk of dying early. Also, ingestion of saturated fats and trans fats (as well as simple sugars) contributes to increased levels of systemic inflammation, which accelerates the diseases of aging.

Alpha-cyclodextrin selectively absorbs and eliminates trans fat and saturated fat before they can enter the bloodstream, while leaving healthy polyunsaturated fats (such as omega-3 fats) available to deliver their benefits. In fact, this fiber binds up to 9 times its weight in health-threatening dietary fat from the intestinal tract. Studies show that, for people who eat two fat-heavy meals a day, 2 grams of alpha-cyclodextrin taken...
before these meals can remove up to **320 calories** from the body before absorption.

Alpha-cyclodextrin has the ability to engulf excess dietary fat, especially pro-inflammatory saturated fat, within the intestine. This fiber has been shown to lower the dangerous apolipoprotein B (apoB) type of cholesterol, elevated levels of which have been shown to contribute to atherosclerosis.26

There have been fat-blocking drugs on the market, but they have been plagued by noncompliance—in other words, users have generally given up on them. Problems with these drugs make them difficult to use. Fat-blocking drugs such as orlistat, which is marketed as Alli® or Xenical®, rely on inhibiting the lipase enzyme that breaks down triglycerides, the major form of dietary fat, into single fatty acid molecules.28 These drugs leave triglycerides “loose” in the colon. There, they may undergo digestion or fermentation to produce gas and fluids, leading to flatulence, urgency, cramping, loose stools, and possibly diarrhea or release of oily material from the rectum.28

Aside from these distressing side effects, there is a nutrition problem related to these fat-blocking drugs. They remove all types of fats, regardless of whether they are good fats or bad fats.

Alpha-cyclodextrin, on the other hand, typically does not have these side effects. Instead of leaving undigested triglycerides “loose” in the colon, this novel compound isolates dietary fatty acids away from the rest of the intestinal contents, thereby reducing the risk of digestive problems.

Because alpha-cyclodextrin does not typically have digestive side effects, there is an increased compliance in taking the product, which translates into reduced markers of cardiovascular and metabolic risk.

**Alpha-Cyclodextrin Reduces Unhealthy Fats**

Japanese researchers have been investigating alpha-cyclodextrin for 30 years since they first established that this novel fiber, when fed to young rats, can effectively modulate lipid metabolism. The result was reduced levels of triglycerides in both blood and liver tissue. The rats also experienced less weight gain and decreased body fat deposition relative to controls that did not receive alpha-cyclodextrin.22

Realization that alpha-cyclodextrin can preferentially reduce unhealthy dietary fats, while leaving healthy fats alone, began when scientists undertook a 14-week study conducted on laboratory mice.28

Scientists fed the mice a high-fat, Western-style diet, but the diets of the test group were supplemented with alpha-cyclodextrin. The supplemented mice
showed decreases of 15.3% in total cholesterol, 20% in free cholesterol, and 14% in cholesterol esters (a bound form of cholesterol). The majority of the cholesterol that was decreased was the dangerous apoB type, known to be increased with the intake of dietary saturated fats and associated with a higher risk of atherosclerosis.26

Critically, measuring the animals’ fatty acid blood levels indicated an even greater reduction in the risk of atherosclerosis and cardiovascular disease. Supplementation with alpha-cyclodextrin had boosted levels of beneficial unsaturated fats by 2.5% while decreasing pro-inflammatory saturated fats and trans fat levels by 4.5% and 11%, respectively.26

In another compelling study, rats were fed diets supplemented with either alpha-cyclodextrin or control supplements. Then, each group was given a diet including radioactively labeled saturated and unsaturated fats. Compared to control animals, the alpha-cyclodextrin group experienced a 7-fold increase in excretion of saturated fats, with no increase in the excretion of beneficial polyunsaturated fats such as omega-3s.29

Following this, a similar experiment provided even further evidence of alpha-cyclodextrin’s preference for blocking the ingestion of unhealthy dietary fats while enhancing beneficial fats.11

In the next section, we’ll examine these impressive findings.
The alpha-cyclodextrin itself caused these favorable shifts in lipid profiles through its remarkable ability to selectively bind and eliminate destructive lipid molecules.

Blocking the absorption of significant quantities of dietary saturated and trans fats and moving this unabsorbed high-calorie fat through the intestinal tract and out of the body would be expected to both promote weight loss and consequently enhance markers of metabolic syndrome. And a further study on rats clearly demonstrated this effect.31

Researchers fed rats a high-fat diet that was supplemented with alpha-cyclodextrin. They found that, as expected, these test animals had a 30% reduction in plasma triglycerides, a 9% reduction in cholesterol, and an increased amount of fat excretion in their feces, again demonstrating successful elimination of unabsorbed fat from the intestine. But additionally, the supplemented animals showed significantly less weight gain despite the high-fat diet than the unsupplemented control animals, all of which gained weight.31

Notably, in this study, the alpha-cyclodextrin group was also found to have improved insulin sensitivity and normalization of serum leptin, the satiety hormone that signals the body that it’s time to turn off feelings of hunger.31

Next, scientists set out to confirm these remarkable effects using the gold standard of scientific evidence: randomized, placebo-controlled human trials.

**Human Studies Show Beneficial Effects**

In a well-designed study conducted on obese patients with type II diabetes, participants gained an average of 2.2 pounds each over a 30-day period prior to the intervention phase. Then, a select group of these participants were randomly assigned to take 2 grams of alpha-cyclodextrin with each fat-containing meal. The rest were given placebos. All volunteers were asked not to change their regular eating habits or daily routine.32

Once the supplementation period began, the placebo group continued to gain weight, but the alpha-cyclodextrin group experienced no further significant weight gain.32

Additionally, the two groups showed notable differences in lipid profiles by the end of the study. Among those who started the study with elevated lipids, the placebo group saw their total cholesterol increase by a substantial 5.2%. In sharp contrast, the alpha-cyclodextrin-supplemented group had a remarkable 8.2% reduction in total cholesterol.32

Furthermore, scientists documented increased levels of adiponectin, a hormone that regulates glucose levels and promotes fatty acid breakdown,
in the alpha-cyclodextrin group, while levels of this beneficial substance fell in the placebo group. Additional evidence of alpha-cyclodextrin’s powerful cardiovascular benefits came from a study enlisting the help of a group of overweight people with a body mass index of 25 to 30 kg/m². They were randomly assigned a placebo or 2 grams of alpha-cyclodextrin with each meal, amounting to 6 grams per day.

After two months, the supplemented individuals showed an array of metabolic benefits. Those taking alpha-cyclodextrin realized an average 5.3% decrease in total cholesterol and an average 6.7% decrease in LDL cholesterol. Compared to controls, supplemented patients’ levels of apoB, an atherosclerosis-promoting protein, fell 5.6%, and their serum insulin levels fell 9.5%.

The beneficial effects shown in these human studies cannot be overstated. Blood triglyceride levels tend to rise very sharply after a fat-heavy meal, and the degree of that increase is a strong predictor of cardiovascular risk. Reducing post-meal triglyceride levels is a critical component of any program for reducing heart disease.

In another study, alpha-cyclodextrin was demonstrated to absorb many times its weight in fat and to sustain its beneficial effects over a prolonged period. Sixty-six obese diabetic patients were randomly assigned to receive either placebo or

Figure 2. Blood sugar levels following “meal” of 100 grams of bread alone or with 10 grams of alpha-cyclodextrin in healthy volunteers. Note the peak rise of blood sugar to 150 mg/dL in control subjects, with gradual rise not reaching 110 mg/dL in supplemented group.

Figure 3. Blood insulin levels following “meal” of 100 grams of bread alone or with 10 grams of alpha-cyclodextrin in healthy volunteers. Note the sharp and early peak in insulin in control subjects, with much lower, later, and less-prolonged elevation in supplemented subjects.
two 1-gram tablets of alpha-cyclodextrin with each meal for three months—a total of 6 grams daily. More weight was lost by those with the highest intakes of total and saturated fats than those with lower intakes. This further confirms that alpha-cyclodextrin preferentially blocks the more dangerous saturated fats and leaves healthy fats alone. Careful analysis also showed that the amount of fat that was excreted by these volunteers was about 9 times the amount of alpha-cyclodextrin that they had ingested, confirming previous laboratory studies.

While these benefits for obese and diabetic volunteers are certainly compelling, the fat-blocking benefits of alpha-cyclodextrin were just as dramatic in healthy individuals. Scientists randomly assigned healthy adult volunteers to take either 2 grams of this novel fiber or a placebo, immediately following a commercially prepared high-fat breakfast rich in saturated fats. Compared to placebo recipients, patients supplemented with this one-time dose of alpha-cyclodextrin absorbed 69% less of the fat provided in the test meal.

**Chewable Tablet**

Both the studies on alpha-cyclodextrin’s carb-blocking effects and on its fat-blocking effects underscore a critical fact. Taking alpha-cyclodextrin before meals can allow individuals to gain control of their metabolic and weight-gain risks as well as their blood lipid and cardiovascular risks.

Alpha-cyclodextrin is best taken in a chewable tablet that allows this unique fiber to be masticated and ready to work once it hits the stomach. Also, in contrast to other less selective, fat-blocking drugs, alpha-cyclodextrin typically has no or few side effects.

**Summary**

Americans typically ingest too many unhealthy sugars, starches, and fats. As a result, they frequently carry around excess abdominal fat, sometimes in spite of their exercise and weight-loss programs.

Scientists have identified a natural fiber called alpha-cyclodextrin that lowers after-meal glucose and insulin surges.

Alpha-cyclodextrin also selectively blocks absorption of unhealthy fats such as trans fats and saturated fats—while leaving beneficial, polyunsaturated fatty acids, such as omega-3s, available to deliver their benefits.

Chewed as a tablet prior to fat-containing meals, alpha-cyclodextrin powerfully improves blood lipids, metabolic and cardiovascular risks, as well as reducing absorption of calories from fat.
If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

References

As one ages, lipids in combination with inflammatory cells, cellular waste products, and calcium build up within the walls of the blood vessels to form arterial plaque.

If this plaque becomes unstable, it can rupture, potentially affecting the vascular endothelium.

The extracts in Arterial Protect have been documented to support the body’s ability to control plaque formation. This plaque can become unstable, potentially affecting the vascular endothelium.¹

Patented and clinically tested, Arterial Protect is a combination of Pycnogenol® French maritime pine bark extract and Centellicum® Gotu Kola leaf extract.

- Pycnogenol® has been demonstrated in controlled research to improve endothelial function and arterial blood flow.² It also significantly reduces oxidative stress. Additionally, Pycnogenol® is known to help modulate healthy inflammation and to help inhibit platelet aggregation.³

- Gotu Kola has been shown in placebo-controlled studies to result in enhanced stability of arterial plaque.⁴,⁵ Gotu Kola modulates production of collagen, which is found in the composition of the cap holding plaque in place.⁴,⁵ It also supports free radical defense mechanisms and helps promote healthy inflammation levels.

When human volunteers were supplemented with both Pycnogenol® and Gotu Kola—the two ingredients in Arterial Protect—progression of arterial plaque was substantially reduced, and this was associated with a reduction in oxidative stress.¹

For those seeking enhanced arterial protection, take just one vegetarian capsule daily of Arterial Protect to naturally stabilize endothelial plaque and promote healthy blood flow.

**References**

To order Arterial Protect, call 1-800-544-4440 or visit www.LifeExtension.com

Arterial Protect
Item #02004 • 30 vegetarian capsules

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Non-GMO
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These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Normal aging and related health issues can decrease production of digestive enzymes, resulting in a bloated feeling and other discomforts after eating a large meal.

Enhanced Super Digestive Enzymes provides specific enzymes required to support the natural reactions that break down food—demonstrated to optimize digestion and nutrient absorption. Here is the broad array of enzymes contained in this formula:

- **Protease** to help break down proteins,
- **Amylase** to break down starch and short sugar chains called oligosaccharides,
- **Lipase** to break down fats,
- **Cellulase** to break down the indigestible polysaccharide in dietary cellulose, and
- **Lactase** to break down lactose.

Enhanced Super Digestive Enzymes with Probiotics provides the same enzymes that are in Enhanced Super Digestive Enzymes—but with the added benefits of the probiotic *B. coagulans*.

This probiotic creates a natural protective shield that resists digestion in the stomach allowing it to fully colonize in the intestines. Probiotics such as *B. coagulans* support digestive health and suppress less beneficial bacteria to improve digestive comfort.

To order Enhanced Super Digestive Enzymes or Enhanced Super Digestive Enzymes with Probiotics, call 1-800-544-4440 or visit www.LifeExtension.com

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**Enhanced Super Digestive Enzymes**

Item #02021 • 60 vegetarian capsules

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**Enhanced Super Digestive Enzymes with Probiotics**

Item #02022 • 60 vegetarian capsules

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**References**

5. Gastroenterology. 1997 May;112(5):1624-34.

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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
After-meal elevations in blood sugar pose a significant risk for the different metabolic challenges that affect millions of Americans today. For those whose changes in diet and lifestyle are not enough to curb after-meal blood sugar spikes, researchers have identified a unique fiber called alpha-cyclodextrin that substantially maintains healthy glucose levels within normal range. In human studies, subjects given alpha-cyclodextrin before carbohydrate consumption showed both healthy blood glucose and insulin response.¹,²

Japanese researchers have identified yet another impressive metabolic benefit of alpha-cyclodextrin.³ This unique fiber selectively absorbs and eliminates bad fats like trans fats and saturated fats before reaching the bloodstream, without affecting the beneficial fats, like omega-3s.⁴

In fact, this fiber binds up to 9 times its weight in unhealthy dietary fat from the intestinal tract.⁴

Alpha-cyclodextrin safely improves metabolic health by maintaining healthy blood sugar levels within normal range and removing harmful fats from the bloodstream.

References
HEALTH RISKS OF COMMON ACID REFLUX MEDICATIONS
Heartburn is defined medically as gastroesophageal reflux disease (GERD).

GERD is caused by the incomplete closure of the sphincter valve between the stomach and the esophagus. This incomplete closure allows harsh stomach contents to reflux back up into the delicate lining of the esophagus, throat, and other tissues.

GERD usually manifests as occasional or chronic pain in the center of the chest and can progress to esophagitis, premalignant changes (Barrett’s esophagus), and esophageal cancer.

Contrary to popular belief, excess stomach acid is not the cause of GERD. Since the advent of drugs such as Nexium®, Prilosec®, and Prevacid®, however, the public thinks all that needs to be done to protect against GERD is to block stomach acid production. This misconception can have deadly consequences.

While proton-pump inhibiting drugs (like Prilosec®) provide merciful relief from the symptoms and some of the pathological effects of GERD, chronic use of these drugs can lead to nutritional deficiencies, bone fractures, and heart disease.

While proton-pump inhibiting drugs impede acid production, they don’t stop the reflux of digestive enzymes, bile, and corrosive food/drinks into the esophageal lining.

Adenocarcinoma of the esophagus has been climbing at an alarming rate and cures elude the majority of patients. Interestingly, this increase in esophageal cancer comes at a time when tobacco use has plummeted.

Tobacco use sharply increases risk of squamous cell carcinoma, but the more prevalent adenocarcinoma is thought to be more related to obesity, which exacerbates the volume of stomach contents that reflux back up into the esophagus.

This article identifies the health risks associated with the overuse of proton-pump inhibiting drugs and provides some alternative treatment considerations.
About 40% of Americans suffer from heartburn attacks every month (with more than 20% experiencing attacks weekly). Long-term therapy is needed for those with more than occasional heartburn.1,2

The danger is that, after prolonged exposure to harsh stomach contents, the cells of the lower esophagus undergo precancerous changes that can lead to esophageal cancer, a growing cause of cancer deaths in older adults.3,4

For chronic GERD sufferers, most physicians prescribe oral drugs that reduce acid secretion in the stomach. Prominent among such drugs are the proton pump inhibitors, which include omeprazole, lansoprazole, pantoprazole, esomeprazole, and rabeprazole, sold under a variety of trade names such as Nexium®, Prilosec®, and Prevacid®.

Unfortunately for GERD victims, long-term use of these drugs brings with them a host of side effects, all related to the drugs’ successful lowering of stomach acid production.

These complications, while not immediately life-threatening, are beginning to concern experts because of their potential impact on quality of life and on long-term health ranging from the heart to the bones and even to the risk for infection, particularly among older adults.

**GERD, Proton Pump Inhibitors, and Long-Term Health**

The human stomach is an extreme environment, constantly churning with muscular action, boiling with hydrochloric acid at a pH near 1, and laden with protein-destroying enzymes. This environment is essential for proper breakdown of large food molecules in preparation for further digestion and absorption in the small intestine. Fortunately, the stomach is well protected against these threats, producing a thick lining of mucus that separates the stomach contents from the delicate walls of the stomach itself.

But the esophagus, the long, flexible tube that connects the mouth to the stomach, lacks protection against acid and other digestive contents. Instead, the esophagus is protected by gravity and a relatively weak sphincter muscle at the lower end of the esophagus to keep stomach contents in place.

After a heavy meal, particularly a fat-rich one that can slow stomach emptying, the pressure in the stomach can overwhelm the lower esophageal sphincter, allowing highly corrosive stomach contents to reflex, or wash back, into the esophagus.5 And many people suffer from transient relaxation of this sphincter, which permits reflux to occur unpredictably.

Symptoms of reflux include the burning sensation referred to as heartburn and are often accompanied by uncomfortable belching and a sour taste in the mouth. Whether it is called heartburn, reflux, or GERD, the condition is both painful and potentially dangerous.

The danger is that, after prolonged exposure to the acids and protein-digesting enzymes in stomach fluid, the cells of the lower esophagus undergo precancerous changes that can lead to esophageal cancer, a growing cause of cancer deaths in older adults.3,4

For chronic GERD sufferers, most physicians prescribe oral drugs that reduce acid secretion in the stomach. Prominent among such drugs are the proton pump inhibitors, which include omeprazole, lansoprazole, pantoprazole, esomeprazole, and rabeprazole, sold under a variety of trade names such as Nexium®, Prilosec®, and Prevacid®.

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**Modern Day Relief**

As a result of all this pain, discomfort, and risk, drug companies, physicians, and patients have eagerly sought a way to reduce the symptoms and cancer threats of GERD. One way of mitigating GERD is to reduce stomach acid production. A number of medications have been developed to do just that, with the category of proton pump inhibitors (PPIs) clearly in the lead.

PPIs work by blocking the action of the cellular “proton pump” in stomach lining cells.8 That pump generates protons (hydrogen ions) from the bloodstream and pushes them out into the stomach.8 The harder that pump works, the more acidic the stomach contents become.
Using one of the PPI drugs reduces the amount of acid that goes into the stomach, which in turn reduces the amount of acid that can reflux, or wash back, into the esophagus to produce heartburn or GERD.9

Proton pump inhibitors do a very good job of reducing symptoms of acid reflux. Such a good job, in fact, that they are the third largest-selling class of drugs, with more than 119 million prescriptions written annually. They generate nearly $14 billion in sales.2,9,10

Originally marketed as prescription drugs for intermittent use, these drugs have been available over the counter for more than a decade, and, though still clearly labeled for limited duration use, many patients with moderate to severe GERD take them as long-term maintenance drugs.2

But, because PPI drugs are so effective at reducing symptoms, and because they are so widely used for such extended periods, some findings are now being reported that were not apparent when these drugs first hit the market.

We should note here that none of the PPI side effects pose immediate, urgent health threats, so it is important that each patient consult with his or her physician about the balance of risks and benefits. Nonetheless, many of the effects of PPIs can, over the long term, raise the risk for significant diseases, such as cardiovascular disease, osteoporosis, infections, and others.2,9,11

What You Need to Know

Health Risks of Proton Pump Inhibitors

- Heartburn or gastroesophageal reflux disease (GERD) is a major problem affecting millions of older Americans.

- The condition is caused by reflux of acidic, enzyme-rich stomach contents flowing backwards out of the stomach and into the esophagus.

- Chronic exposure to stomach contents can alter the esophageal lining, eventually making it cancer-prone.

- Reduction of GERD symptoms and effects is therefore an important part of modern medicine.

- A highly effective class of drugs called proton pump inhibitors (PPIs) has emerged. PPIs are capable of suppressing stomach acid production and mitigating symptoms.

- Large numbers of people are now using PPI therapy for prolonged periods, leading to unanticipated consequences.

- These consequences include diminished absorption of vitamins and minerals, poor bone quality, and an increased risk for fracture and even cardiovascular abnormalities that can increase the risks of heart attack or stroke.

- Several natural supplements are now available for people who take PPIs but want to reduce their risk.

- Other supplements may help individuals avoid use of PPIs entirely, because they suppress GERD symptoms effectively on their own.
PPIs Interfere with Vitamin and Mineral Absorption

**Vitamin B12**, like most vitamins, must be obtained from the diet, where it is bound to proteins. Deficiencies in vitamin B12 can produce anemia, depression, and disrupted nerve signaling (including decreased taste and numbness or tingling in the extremities).

But an acidic stomach environment is essential for proper vitamin B12 absorption because the acid is required to break down dietary proteins to which the vitamin is bound, and release it for absorption. Reducing stomach acid, especially by proton pump inhibitors, is likely to interfere with our ability to extract vitamin B12 from our foods.

Studies show that most oral acid-suppressing medications, including PPIs, decrease absorption of vitamin B12 from foods. In one compelling study, 75% of PPI users were deficient in vitamin B12, compared with just 11% in non-users, a significant difference. Other studies document a nearly 4-fold increase in the risk of B12 deficiency among users of oral acid suppressant drugs, both PPIs and H2 blockers, now a second-line drug.

Experts recommend that, based on current information, people taking PPI therapy for long periods should have their vitamin B12 levels checked and consider supplementation. Vitamin B12 supplied as a crystalline supplement appears to be better absorbed in people taking PPIs than is vitamin B12 supplied in food. That is because it does not have to be separated from foods in the stomach.

**Iron** is an essential nutrient, especially for formation of red blood cells and proper muscle function. Like vitamin B12, stomach acid is an important requirement for proper absorption. That’s because about one-third of our iron intake comes from non-animal sources, where it is bound to plant chemicals that inhibit its absorption, while stomach acid breaks down those inhibitory molecules. This problem is especially important in people who eat little to no meat, since obviously the proportion of iron from plant sources they receive is considerably larger.

Furthermore, studies show that people with conditions that naturally produce low stomach acid concentrations, a condition known as hypochloridia, have difficulty absorbing iron, and are more prone to developing iron-deficiency anemia. And animal studies verify that PPI treatment decreases iron absorption, particularly in animals on a low-iron diet. Some human studies demonstrate that long-term PPI use reduces iron absorption and produces the expected biochemical disturbances in blood tests. Indeed, for patients with a problem storing too much iron, which results in tissue toxicity, PPI therapy has been deliberately used to reduce dietary iron absorption, demonstrating the potency with which these drugs can interfere with iron metabolism.

**Magnesium** is another essential mineral that is important for the functioning of numerous enzyme systems, energy management, and nerve conduction. Deficiency of magnesium is surprisingly common, with just 32% of Americans meeting their daily recommended intake. There have been reports of low blood magnesium levels in chronic PPI users. One review study found severe symptoms of low magnesium, including fatigue, unsteadiness, numbness/tingling, seizures, heart rhythm disturbances, and hospitalization, in people who had been taking PPIs for an average of just over eight years. When PPI therapy was stopped in these patients, magnesium levels returned to normal and symptoms resolved, but when therapy was once again started, low levels and symptoms recurred.

PPIs Increase Risk of Bone Fractures

Possibly as a result of disturbances in calcium absorption from the diet under conditions of low stomach acid, a growing number of studies show an increased risk of bone fractures in long-term PPI users.

It is known that stomach acid secretion can boost calcium absorption, while acid-suppressive therapy, including PPIs, reduces such absorption, with a negative impact on bone mineral density. As with the other nutrients, stomach acid facilitates release of calcium from its dietary form, allowing it to be absorbed, so reducing acid levels will reduce the amount of dietary calcium that reaches the bloodstream and eventually the bones.
In one study of people older than 50, the use of PPIs for more than a year was associated with a 44% increase in hip fracture risk. In that study, the risk of fractures was significantly higher (165%) in people taking doses above 35 mg (the average daily dose is 20 mg), and the risk continued to escalate the longer the patients took the PPI medication.

Another study showed similar results on the risk of hip fractures (increased by 45%), though neither dose nor duration appeared to have an effect in this case. And a still more strongly designed study demonstrated, among postmenopausal women, a 3.1-fold increased risk for spinal fractures in PPI users compared to non-users.

Taken together, these studies and others have led the US Food and Drug Administration (FDA) to warn users of PPIs of a “...possible increased risk of fractures of the hip, wrist, and spine with high doses or long-term use of a class of medications called proton pump inhibitors.” The required product labeling was also changed to reflect this increased risk.

PPIs and Cardiovascular Risk

Despite some encouraging trends in recent years, cardiovascular disease (heart attacks, heart failure, strokes) remains the leading cause of death in American men and women. The use of PPI medications is emerging as one such risk factor.

There are two major ways that PPI therapy raises cardiovascular risk. The first has to do with PPI effects on blood clotting systems, particularly on platelets, the tiny cell fragments that initiate a clot. Most patients who are known to be at elevated risk for heart attack or stroke are placed on some kind of antiplatelet medication to lower their likelihood of developing an artery-blocking clot.

Because antiplatelet medications raise the risk for bleeding and ulcer formation in the stomach, however, most such patients are also advised to use a PPI to suppress stomach acid and decrease the risk of catastrophic bleeding. But recent studies now suggest that the PPI medications may inhibit the effectiveness of the antiplatelet drugs themselves, defeating the entire purpose of this multidrug cocktail.

This effect is especially important with the antiplatelet drug clopidogrel (Plavix®), which requires activation in the liver by a specific enzyme (CYP2C19). PPI drugs, particularly omeprazole, interfere with that enzyme’s activity, hence reducing the amount of active clopidogrel available to prevent platelet clotting.

These biochemical effects have real impact on human lives. Studies now reveal a variety of negative effects among people with heart attack risk who take PPI medication along with antiplatelet therapy:

- Increased risk of cardiovascular “events” (e.g., heart attacks, need for interventional surgery),
- Increased risk of dying from a major acute cardiac event (in high-risk patients),
- Increased risk for recurrent attacks of acute coronary syndrome (angina, heart attacks), and
- Increased risk of re-infarction (death of heart tissue) after treatment for a first infarction.
Periodically checking iron and magnesium levels, and supplementing with these minerals if levels are borderline or low.

Monitoring bone mineral density for evidence of developing osteoporosis, with appropriate supplementation with calcium and vitamin D as required.

Taking pomegranate extracts to protect nitric oxide from oxidative destruction, and thus improving otherwise impaired endothelial function resulting from PPI use.39

Other people, particularly those with milder or more intermittent episodes of heartburn/GERD, should explore natural alternatives to PPI medication. This may help them sidestep the increased risks entirely.

Among good choices are:

- **Raft-forming alginates.** These are acid-activated gels that form a foamy “raft” that floats on top of stomach contents. They have the advantage of blocking not only stomach acid, but also destructive protein-degrading enzymes from rising into the esophagus.40-42 Use raft-forming alginates to take a break from PPIs, while also sparing the esophagus from other corrosive digestive stomach contents (enzymes, bile, food and drink).

The second, independent way that PPI drugs may increase risk of cardiovascular disease is their impact on production of artery-relaxing **nitric oxide.** The cells that line the blood vessels (endothelium) produce nitric oxide as a signaling molecule that tells arterial wall muscles to relax, allowing increased blood flow to oxygen-hungry tissues, particularly the brain and heart. Healthy nitric oxide production means brisk and efficient control of blood flow in these vital organs.

Recent studies show that PPI drugs lead to a reduction in nitric oxide, producing sluggish responses by arteries to the need to increase blood flow, and an increase in the risk of an infarction, ultimately producing a heart attack, stroke, or other catastrophe.9

**How Nutritional Supplementation Can Help**

Clearly, one needs to balance the benefits provided by effective heartburn medications against the risks of long-term use. For some people, the decision may be to continue using PPI medications periodically, while attempting to lower some of the risks we’ve identified above. Some ways to do that include:

- Having a vitamin B12 level checked regularly, and supplementing with B12 in the event of low or borderline levels. Remember that, unlike B12 from foods, reduced stomach acid does not appear to impair absorption of crystalline B12 from supplements.2 A blood test for B12 should nonetheless be done when using PPIs and if there is a B12 deficiency, then ask your doctor to prescribe a B12 shot (1 mg) to be injected into a muscle two to three times a week.
• **Monitor meal size and macronutrient composition.** Dietary fat delays gastric emptying, which may increase the probability of reflux in susceptible patients. High-fat meals are also associated with increased risk of esophageal cancer.\(^\text{52}^\) Whereas high-calorie, high-fat meals appear to elicit GERD,\(^\text{53,54}\) reducing fat content in meals has had beneficial effects in some studies.\(^\text{55,56}\) Low-carbohydrate (< 20 gram) meals reduced some reflux symptoms in a small trial in obese subjects.\(^\text{57}\) Aside from their direct effects on GERD, limitation of fat, carbohydrate, and total calorie intake are effective methods for weight reduction, which itself is an effective anti-reflux strategy. Weight reduction is also an effective way to positively impact many additional aspects of health and potentially enhance longevity.

• **Avoid eating close to bedtime.** GERD patients have long been advised to avoid eating close to bedtime in order to give the stomach adequate time to empty before lying down.\(^\text{58}\) Clinical studies, however, have had mixed results regarding the minimization of GERD symptoms.\(^\text{59-61}\)

• **Elevate the head of the bed while sleeping.** Several studies have suggested that raising the head of the bed 8-11 inches, or sleeping on a “wedge,” can reduce the number and duration of reflux episodes.\(^\text{62}\) This approach uses gravity to help keep stomach contents out of the esophagus. Left lateral recumbency (sleeping on the left side) may also reduce GERD symptoms by potentially keeping the lower esophageal sphincter above the level of the stomach and reducing pressure on the valve.\(^\text{62}\)

• **Limit aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs).** Some evidence suggests that NSAID use is associated with GERD.\(^\text{63}\) NSAIDs exert their anti-inflammatory activity by inhibiting the activity of pro-inflammatory cyclooxygenase (COX) enzymes. However, the COX-1 enzyme is also important for promoting the formation of the protective mucus lining of the stomach.

• **Avoid foods and beverages associated with GERD symptoms.** This includes coffee, chocolate, spicy foods, carbonated beverages, and alcohol. Additional foods that may cause symptoms include tomatoes (cooked and raw), milk, cheese, citrus foods, cakes, and pastries.\(^\text{43-48}\)

• **Quit smoking.** According to a long-term study, daily long-term (20 plus years) smoking resulted in a 70% increase in the occurrence of reflux episodes compared to those who smoked less than a year.\(^\text{49}\)

• **Lose weight.** Increased body mass and abdominal adiposity increases pressure on the stomach and lower esophagus. This can stress the lower esophageal valve, hampering its ability to maintain a seal against gastric reflux. Sustained abdominal pressure can also increase the risk of hiatal hernia.\(^\text{50}\) Based upon a survey of seven studies, overweight individuals averaged a 43% increase and obese individuals a 94% increase in GERD symptoms over individuals with a normal body mass.\(^\text{51}\) Esophageal adenocarcinoma incidence was more frequent in overweight individuals in most of these studies.
Loss of control of the lower esophageal sphincter muscle results in painful heartburn, also known as GERD. GERD affects millions of people, particularly older adults, and most of those people turn to oral acid suppressive medications for relief.

The leading acid-suppressing drugs are in the category of proton pump inhibitors, which are known to be highly effective at reducing heartburn symptoms. But these drugs, called PPIs, are proving to have concerning side effects, particularly when used over the long term. Reduced acid secretion in the stomach can impair absorption of essential nutrients like vitamin B12, and minerals, such as iron, magnesium, and calcium.

Poor calcium absorption and other effects of PPI use raises the risk for bone fractures, already a major concern among older adults.

And, by at least two independent mechanisms, PPIs are associated with elevated risk for cardiovascular disease and even death from these conditions. PPIs impair the actions of antiplatelet drugs used to reduce the risk of clotting, and they also inhibit normal production of nitric oxide, a signaling molecule vital for normal blood vessel function.

Some people may choose to accept the risk of PPI medication in light of their substantial symptom relief. For those people, supplementing with vitamin B12 and pomegranate may help to offset some of the risks.

Other people may wish to use heartburn-reducing therapy that does not involve PPI medications at all. Such therapies include raft-forming alginates, which physically block stomach contents from rising up the esophagus.

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

References


Profound shrinkage of synaptic connections between nerve cells is one of the major hallmarks associated with brain aging. Magnesium is a critical factor in controlling synaptic density in the brain.¹

An innovative form of magnesium called Neuro-Mag® has been shown to specifically target multiple areas of the aging brain. In fact, preclinical models show that the magnesium-L-threonate contained in Neuro-Mag® boosted levels of magnesium in spinal fluid by 15% versus no increase from conventional magnesium.² This means that this form of magnesium is passing through the blood-brain barrier for assimilation into the brain.

Comprehensive Cognitive Benefits

Scientists continue to uncover magnesium’s comprehensive benefits for cognitive function.³ Studies using magnesium-L-threonate show this unique form of magnesium maintains the quantity of synaptic connections between brain cells and inhibits the dysregulation of signaling pathways.¹

Neuro-Mag®...Capsules or Powder

The suggested daily dose of three Neuro-Mag® capsules provides 2,000 mg of Magnesium-L-Threonate. While supplying a modest 144 mg of elemental magnesium, its superior absorption into the bloodstream and nervous system make it a preferred choice for maturing individuals to supplement with.

This same brain-health supporting magnesium is also available in a powder called Neuro-Mag® Magnesium-L-Threonate with Calcium and Vitamin D³. In addition to its fresh lemon flavor, the one-scoop-per-day serving supplies the same amount of magnesium as the capsules, plus 500 mg of highly soluble calcium and 1,000 IU of vitamin D³.

References

Immediate Relief for Esophageal Distress

Nearly 60% of adult Americans suffer some form of gastroesophageal upset\(^1\)—and find little relief in commercial products.

Fortunately, a unique compound known as raft-forming alginate produces a temporary physical barrier between the stomach and the esophagus,\(^2\) helping to protect the delicate esophageal tissue from harsh stomach acids.

A unique blend of ingredients in Esophageal Guardian, including alginic acid and potassium bicarbonate, produces both a gel and bubbles to form a safe, protective floating foam layer that sits above the contents of the stomach.\(^2\)

Two other ingredients in the formulation—calcium carbonate and magnesium carbonate—react with the stomach acid to help neutralize it.\(^2\)

Clinical studies show this temporary foam barrier provides maximum support for delicate esophageal tissues.\(^2,3\)

This barrier develops in under a minute, yet relief lasts up to four hours!

The suggested dose of two Esophageal Guardian Natural Berry Flavor chewable tablets provides:

<table>
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<td>35 mg</td>
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To order Esophageal Guardian Natural Berry Flavor, call 1-800-544-4440 or visit www.LifeExtension.com

References
Omega-7
With Highly Purified Provinal® Fish Oil

As a Life Extension® customer, you most likely take an omega-3 supplement. Scientists are increasingly excited about the newly discovered effects of another family of beneficial fats—omega-7 fatty acids.

Omega-7 palmitoleic acid powerfully complements omega-3 fatty acids with cellular-signaling properties that support healthy metabolic factors associated with:

- Superior cardiovascular health¹ ²
- A healthy inflammatory response³ ⁴
- Optimum normal metabolism of glucose and insulin⁵ ⁶ ⁷
- Beneficial management of hunger and satiety⁸ ⁹

Scientific studies show that palmitoleic acid promotes healthy levels of triglycerides, total cholesterol, LDL, and HDL for those already in normal range—after just one month of supplementation at 210 mg.⁹

Further studies have found within normal range, palmitoleic acid can help balance C-reactive protein levels,⁹ optimize insulin sensitivity,¹⁰¹¹ and regulate hunger-promoting gastric hormones.⁹ ¹²

Life Extension®’s omega-7 supplement contains Provinal®—a highly refined anchovy and/or menhaden oil that is non-GMO. Conventional processing methods result in products with only 25% palmitoleic acid. Life Extension®’s Provinal® Purified Omega-7 is concentrated to 50% palmitoleic acid.

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These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Cheryl Martin faced death four times, yet managed to survive. Perhaps it was these experiences that eventually led to a life of helping others get healthy. And while her childhood dream of practicing medicine was put aside for marriage and children, her love of healing was always waiting in the background. Today Martin is the owner and director of the Gardens Wellness Center in Palm Beach Gardens, Florida, where she lives a fulfilling life restoring good health to her many patients.

Beginning

Martin was born premature and as an infant, almost didn’t survive. Martin’s mother was advised not to get too attached to her daughter since she was probably not going to live. Martin surprised everyone by coming through, despite clinically dying several times.

But being born premature was only the first of Martin’s many near-death experiences: She almost died from a misdiagnosed thyroid problem, suffered a carotid aneurysm, and was one inch from being killed in a head-on auto collision. If anything, she is a true survivor.
The dynamic and multitalented Martin has worked in numerous professions during her adult life, including real estate, marketing, web design, TV host, and executive producer. She became involved in the Gardens Wellness Center prior to its opening and decided it was the one place she desperately wanted to be. Over the years, Martin acquired expert education and training in a variety of disciplines, including neuro-linguistic programming, hypnotherapy, massage, cognitive behavioral therapy, and life coaching. She also trained as a midwife and periodically works as a doula or a midwife’s assistant. She radiates boundless energy and a true gift for healing.

Gardens Wellness Center

A one-stop facility for a wide variety of holistic approaches, the Gardens Wellness Center focuses on not only alleviating symptoms but on finding and treating the cause of a person’s illness. The practice provides acupuncture, chiropractic care, functional medicine, hormone replacement therapy, colon hydrotherapy, nutritional counseling, herbal prescriptions, detoxification, hypnotherapy, reiki, massage, reflexology, and more. Common conditions that are treated include endocrine and hormone disorders, infertility, migraines, pain management, and orthopedic and sports issues. The majority of patients have been referred by their doctors, while others have come because they are disillusioned with the traditional treatments they’ve received. The Center’s aims are to prevent disease and heal or improve existing conditions, bringing patients to the healthiest state possible.

“The typical patient comes in with a modality already in mind,” says Martin. “They will say, ‘I’m in pain, so I want acupuncture,’ or ‘I had a car accident and I need chiropractic.’” On every initial visit, Martin reviews the health history of new patients and consults with a health practitioner regarding a treatment plan. She continues to follow up by going over patient charts, diagnoses, and treatments to make sure each person is healing and progressing. She and her team work harmoniously to provide for each patient’s optimal outcome. Every person that comes through the door is evaluated physically, mentally, nutritionally, and spiritually. The team at Gardens Wellness Center embraces the patient’s unique needs and treats the patient for each of the deficiencies they present with.

“For example,” Martin says, “if someone is on a medication with the side effect of decreasing bone mass, I’ll explain that they need a very high calcium supplement. Then I explain that if [they] take the calcium, it may not absorb properly in the bones and might get into the soft tissue, so [they] also need vitamins D3 and K2 to transport the calcium, break it down, and make it available to the bone. They’ll also need magnesium or the body won’t be able to utilize it. In a case like this, the patient will go home with Life Extension® Bone Restore and won’t have to buy many different separate products.

“We do not take someone for just one treatment, unless they’re only coming in to treat stress,” Martin adds. She tells people who think they can fix everything in one visit, “We’re not going to take your money, because it may have taken you seven years to develop your condition and one treatment is not going to fix it. You will need seven to 14 treatments before we see changes in your body.” Once they understand, patients almost always comply.
Acupuncture for chronic pain is very popular at the Center and Martin explains how the body and acupuncture work together to heal an old injury. “When something acute happens in your body,” she tells patients, “your body immediately [focuses] its attention on repairing that injury. But after some time, your body will get busy with fighting an illness or tending to another problem and will ignore and forget your first injury.” The result, she explains, can be permanent pain, inflammation, and loss of motion. Acupuncture treatment at the site of chronic pain re-activates your body to go back and heal old injuries, as well as restore motion and wellness.

One of Martin’s favorite referrals following treatment was from a recent patient who told her that he felt like the Tin Man from “The Wizard of Oz,” and that every movement hurt. “He told me, ‘I feel like you guys added oil to my joints. I’m working out at the gym now, which I couldn’t do a month ago.’”

Counseling diabetics to stay away from sugar is also complex, Martin notes, because carbohydrates turn into sugar and “a diabetic has to know that you can’t eat a 12-inch sub and potato chips and think that’s [better than] eating two pieces of cake, because they both end up having the same result.” The Center teaches patients carb counting and to consume enough carbs before exercising, especially if patients are on insulin, and how to get obesity under control, which often cures adult onset diabetes. They also recommend that some people, regardless of weight, take insulin because their bodies simply do not produce enough naturally.

“A lot of diabetics are in complete denial,” Martin observes, “and it’s so important for them to understand how to manage their condition properly.”

Martin recalls a diabetic who told her, “I’ve tried to change my diet, but I can’t, so I’m just going to live this way and die early because I can’t control myself. I like my cakes and cookies too much.”

Using hypnotherapy, Martin induced the patient to choose healthy snacks instead of sweets, and after a few treatments, the patient stopped eating sweets nightly.

Martin’s favorite story is about her first stroke patient who came on a referral from a neurologist who believed hypnotherapy could restore some movement in her curled arm and fingers, which were barely moving. Martin says that each patient receives an individualized treatment plan, and in this case, she was uncertain about how to proceed. Her research found information that “you can use the mind to tell the arm that it is lifting weights or heavy objects and that will actually strengthen the muscles.”

During a hypnotherapy session, Martin had the patient imagine lifting her purse with her affected arm. Martin observed the patient’s fingers moving in a way they had not moved before hypnosis. “I’m watching her fingers [move] and the muscles tighten in her arm,” she says, “and I’m thinking that
this is phenomenal.” This patient made remarkable improvements and Martin says she feels elated at being able to change a life so profoundly.

Martin also mentions the powerful effect that stress can have on physical health. “Emotions can make you sick,” she explains. “The same hormones, cortisol and adrenaline, that are responsible for motivating us to run from real danger can cause damage when we experience emotional problems. In the former case, they can save your life, while in the latter case, they can kill you.”

Many people develop what’s called a stress belly, Martin explains. The body stores fat in the abdomen because it’s saving its use as energy to fight whatever is elevating stress hormones. The danger comes when the body cannot find a cause for the elevated hormone levels so it starts to search the DNA. When that happens, it can trigger damaged dormant cells like cancer cells. All of this is due to stress. “Living a stressful life will eventually kill you,” Martin concludes.

For overly stressed patients, Martin recommends acupuncture, life coaching, hypnosis, cognitive behavioral therapy, and biofeedback to help patients learn calmness and retrain their thinking. Martin mentions that all these therapies are blended, each mode combining with the others, strengthening one another. Ultimately, the mind soothes the body.

**Martin’s Personal Care**

Martin herself eats a low-carbohydrate diet, avoiding bread, sugar, and processed foods. Her diet consists of fruit, vegetables, lots of fish, and some poultry. Martin recommends that her patients avoid the center aisles of a grocery store where all of the processed and packaged items exist. Sticking to the outer perimeter provides everything your body needs.

A strong advocate of Life Extension, Martin takes a variety of products, including those for healthy hair and skin. For exercise, she gets to the gym whenever possible and loves taking long walks after dinner.

Martin also takes her own advice and seeks regular care from both Western and alternative practitioners to be certain that her body is in optimal condition. She mentions that the staff at the Wellness Center often treat each other and that there is a wonderful feeling of harmony as they strive to bring good health to all their patients and to each other.

**Advice to Others**

“People take less care of themselves than they do of their vehicles or their homes,” Martin observes. She says many people spend enormous amounts of money on vacations, eating out, and buying clothes, then tell themselves they can’t afford to go to a doctor or dentist. She hopes people will examine how they are living and realize that health comes before anything and everything else.

“People assume that if they’re feeling okay, nothing’s wrong. But you have to take care of your body the same way you would get an oil change in your car. The biggest thing I could tell anyone is take care of your health, take care of your body, take care of your teeth.” This means regular, frequent checkups with both Western and holistic practitioners. “Take care of yourself.”

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

For more information or to contact Cheryl Martin, visit www.gardenswellness.com
Author, journalist, explorer, and health activist Dan Buettner has traveled the world investigating unique areas—known as Blue Zones—where people live extraordinarily long and healthy lives. In his new book *The Blue Zones Solution: Eating and Living Like the World’s Healthiest People*, a follow-up to his bestselling book *The Blue Zones: Lessons for Living Longer From the People Who’ve Lived the Longest*, Buettner describes the eating habits and lifestyle choices that allow people from these five areas—including locations such as Okinawa, Japan, Sardinia, Italy, the Nicoya Peninsula of Costa Rica, Ikaria, Greece, and Loma Linda, California—to live well into their 80s, 90s, and 100s—all the while enjoying vibrant good health and a full and happy life.

Most people living in Blue Zones enjoy physical activity incorporated naturally into their daily lives (like gardening or walking), a sense of purpose (like caring for grandchildren or volunteer work), low stress levels and a slower pace of life, strong family and community connections, and a diet characterized by moderate caloric intake, mostly from plant sources.
While there are certain key characteristics that comprise a Blue Zone, such as eating a plant-based diet and engaging in daily activity, “It’s not a silver bullet,” said Buettner, in an interview with CBS news. “It’s silver buckshot. We found nine common denominators of the world’s longest living. When it comes to diet, there’s a big argument for having a vegan diet, but we find that by looking at data from 100,000 Americans, the Adventist health study, that adding a little bit of fish to your diet, being a pescatarian, is actually better for you.

“If you can articulate your sense of purpose, it’s worth about eight extra years of your life expectancy.”

LE: Longevity—as well as the good health to enjoy those extra years—is vital to Life Extension® readers. You’ve explored the earth finding pockets of healthy longevity and the secrets that make these people some of the longest-lived on the planet.

DB: For more than a decade, I’ve been working with the National Geographic Society to identify hot spots of longevity around the world—areas we called Blue Zones because a team of researchers had once circled a target region on a map with blue ink. Teaming with demographer Michel Poulain, I set out to find the world’s longest-lived people. We wanted to locate places that had not only high concentrations of 100-year-olds but also clusters of people who’d grown old without diseases like heart problems, obesity, cancer, or diabetes. We found five places.

1. Ikaria, Greece, an island eight miles off the coast of Turkey that has one of the lowest rates of middle-age mortality and the lowest rates of dementia,

2. Okinawa, Japan, home to the world’s longest-lived women,

3. Ogliastra Region, Sardinia, Italy, the mountainous highlands of an Italian island that boasts the world’s highest concentration of centenarian men,

4. Loma Linda, California, a community with the highest concentration of Seventh-Day Adventists in the US, where some residents live 10 more healthy years than the average American,

5. Nicoya Peninsula, Costa Rica, in Central America where residents have the world’s lowest rates of middle-age mortality and the second highest concentration of male centenarians.

LE: Despite the fact that these locales are spread around the globe, there must have been one or more common denominators. What longevity factors did these five location have in common?

DB: Remarkably, no matter where I found long-lived populations, I found similar habits and practices at work. When we asked our team of experts to identify these common denominators, they came up with nine lessons, which we call the Power Nine. They include moving naturally, purpose, downshift, the 80% rule, plant slant, wine at 5:00, right tribe, community, and loved ones first.

LE: Please explain each of these nine rules in more detail.

DB: [The first] is move naturally. The world’s longest-lived people don’t pump iron, run marathons, or join gyms. Instead, they live in environments that constantly nudge them into moving. They grow gardens and don’t have mechanical conveniences for house and yard work. Every trip to work, to a friend’s house, or to church occasions a walk.

Purpose—the Okinawans call it Ikigai and the Nicoyans call it Plan de Vida, which both translate to “why I wake up in the morning.” In all Blue Zones, people had something to live for beyond just work. Research has shown that knowing your sense of purpose is worth up to seven years of extra longevity.

Even people in the Blue Zones experience stress, which leads to chronic inflammation associated with every major age-related disease. These people have routines to shed that stress [or downshift]. The Okinawans take a few moments each day to remember their ancestors, Adventists pray, Ikarians nap, and Sardinians do happy hour.

The 80% rule reminds people to stop eating when their stomachs are 80% full. Hara hachi bu is a 2,500-year-old Confucian mantra said before meals on Okinawa [to remind themselves of this]. The 20% gap between not being hungry and feeling full could be the difference between losing weight and gaining it. People in the Blue Zones eat their smallest meal in the late afternoon or early evening, and then they don’t eat any more the rest of the day.

Meat—mostly pork—is eaten on average five times a month in a serving of three to four ounces, about the size of a deck of cards. Beans, including fava, black, soy, and lentil—the plant slant—are the cornerstone of most centenarian diets.

Wine at 5:00. People in all Blue Zones (even some Adventists) drink alcohol moderately and regularly. Moderate drinkers outlive nondrinkers. The trick is to drink one or two glasses per day with friends and/or food. And no, you cannot save up all week and have 14 drinks on Saturday!
The world’s longest-lived choose or were born into social circles, the right tribe, that support healthy behaviors. Okinawans create moais—groups of five friends that commit to each other for life. Research shows that smoking, obesity, and even loneliness are contagious. By contrast, social networks of long-lived people favorably shape their health behavior.

All but five of the 263 centenarians interviewed belonged to a faith-based community. Denomination doesn’t seem to matter. Research shows that attending services four time a month will add four to 14 years of life expectancy.

Successful centenarians in Blue Zones put family or loved ones first. They keep aging parents and grandparents nearby or in the home, which lowers disease and mortality rates of their children. They commit to a life partner (which can add three years of life expectancy) and they invest in their children with time and love, which makes the children more likely to be caretakers when the time comes.

LE: Let’s delve into some of the unique health habits of each Blue Zone area. The Mediterranean Diet is something Life Extension® has long recommended as a key to good health and an increased life span. It’s a diet that the centenarians on the Greek island of Ikaria have followed for centuries.

DB: Like other Blue Zones, Ikaria is remote and people have stuck to their traditions, which have enabled them to avoid the influence of modern Western eating habits. Their tradition of preparing the right foods, in the right way, has a lot to do with the island’s longevity.

The island’s diet, like much of the Mediterranean, includes lots of vegetables and olive oil, smaller amounts of dairy and meat products, and moderate amounts of alcohol. What sets it apart from other places in the region is an emphasis on goat’s milk, legumes (especially garbanzo beans, black-eyed peas, and lentils), wild greens, some fruit, and relatively small amounts of fish.

LE: What is it specifically about eating or not eating these foods that increases longevity?

DB: Low dairy consumption has been associated with reduced heart disease. Olive oil, especially unheated, is believed to lower bad cholesterol and increase good cholesterol. Goat’s milk contains serotonin-boosting tryptophan. And wine, in moderation, helps the body absorb more of the flavonoids from the food eaten with it. Black-eyed peas, rich in protein and fiber, have been found to contain some of the strongest anticancer, antidiabetes, and heart-protective substances in nature.

LE: Wild greens and lemons are also on the list of top longevity foods from Ikaria.

DB: Wild greens, such as purslane, dandelion, and arugula, grow all over the island. These wild mountain greens are a great source of minerals like iron, magnesium, potassium, and calcium as well as carotenoids [that] the body converts to vitamin A. Eating a cup daily seemed to be one of the keys to longer life in Ikaria.

IKarians put lemon juice on everything. They eat the whole fruit, skin and all. The high acidity of lemon peels may have a beneficial impact on blood sugar, helping control or prevent diabetes.

LE: You traveled to Okinawa, Japan, where you interviewed a centenarian you describe as having the flexibility of a yogi and the frenetic energy of a Chihuahua. It took some doing, but you finally convinced her to share her secrets.

DB: It took two days to convince [104-year-old] Gozei Shinzato to show me her arsenal of longevity supplements, but in the end she delivered. She showed me one supercharged supplement with carotenoids, flavonoids, and saponins, and another that fights breast cancer by reducing blood estrogen. [She showed me] a proven antimalarial agent to keep her stomach healthy, another to help regulate metabolism, maintain low blood pressure, and treat gallstones. [Another] lowers blood sugar to help stave off diabetes.

The “supplements” on display were Okinawan sweet potatoes, soybeans, mugwort, turmeric, and goya, a bitter melon. All grew 15 feet from her house.

LE: Another top longevity food of the Okinawans is seaweed. Along with turmeric and sweet potato, these three foods provide additional benefits for delaying aging. Can you please explain?

DB: They mimic calorie restriction, a digestive survival mode with longevity benefits. As food is digested, mitochondria in our cells convert calories to energy.
A by-product of this process are free radicals, oxidizing agents that deteriorate the body from the inside out. Free radicals stiffen arteries, shrink the brain, and wrinkle skin. In calorie restriction mode, our cells protect themselves by producing less energy but also throwing off fewer free radicals and thus slowing the aging process.

Recent research...has shown that regular consumption of turmeric, sweet potato, and seaweed can provide some of the benefits of calorlc restriction, tripping genetic triggers that minimize production of free radicals without causing hunger.

**LE:** You mentioned bitter melon as a staple of the Okinawan diet. What is this?

**DB:** It’s not a fruit—it’s a long, knobby gourd. It’s often served with other vegetables in a stir-fry. Recent studies found it an effective antidiabetic as powerful as pharmaceuticals in helping regulate blood sugar. Like the sweet potato, turmeric, and seaweed, it contains chemicals that may slow the production of corrosive free radicals. It’s becoming more and more available in American gourmet produce markets [and] there is nothing quite like it as a substitute.

**LE:** I was somewhat surprised that an American community is included in the Blue Zones. Yet the Seventh Day Adventists in Loma Linda, California, live an average of 10 years longer than the typical American life span of 79 years.

**DB:** These are Americans... They live among us, drive by the same fast-food restaurants, shop in the same grocery stores, breathe the same air, and work the same jobs. But they’re living a decade longer!

The first Adventist Health Study, the AHS-1, funded by the National Institutes of Health, followed 34,000 Adventists in California for 14 years. In that study, [it was found] that Adventists who most strictly followed the religion’s teachings lived longer than people who didn’t. The practices most likely to yield that longevity, each adding about two years to life expectancy, are eating a plant-based diet with only small amounts of dairy or fish, not smoking, maintaining medium body weight, eating a handful of nuts four to five times a week, and doing regular physical exercise.

**LE:** Adventists support their diet by citing Genesis 1:29: “And God said, Behold, I have given you every herb bearing seed, which is upon the face of all the earth, and every tree, in which is the fruit of a tree yielding seed; to you it shall be for meat.”

**DB:** The Adventist encourage a well-balanced diet including nuts, fruits, and legumes, low in sugar, salt, and refined grains. Their diet prohibits foods deemed unclean by the Bible, such as pork or shellfish. The only beverage endorsed is water—at least six glasses a day.

**LE:** What are some more of the Adventists’ top-longevity foods?

**DB:** Avocados, which may help reduce blood pressure and the risk of stroke. Salmon—people who eat one to two three-ounce servings weekly of fish rich in omega-3 fatty acids reduced their chance of dying from a heart attack by a third. A [1990s] study found that Adventists who ate a handful of nuts at least five times a week lived two to three years longer than people who didn’t eat nuts. More research since then found links between nut eaters and lower rates of cholesterol, blood pressure, chronic inflammation, diabetes, and a myriad of other troubles that add up to cardiovascular disease. Beans and other legumes represent [their] daily protein source, and a staple is slow-cooked oatmeal, [which] provides a balanced portion of fats, complex carbohydrates, and plant protein, along with good doses of iron and B vitamins. Its high fiber makes it filling, and nuts and dried fruits add fiber, flavor, and variety. Whole-wheat bread and soy milk are also included.

**LE:** Research has found that Costa Ricans living on the Nicoyan peninsula have the longest life expectancy of anyone in the world.

**DB:** Today, [Nicoyan] middle-aged people—especially men—reach a healthy, vital age of 90 at rates of up to 2.5 times greater than those in the US. In other words, residents here elude heart disease, many types of cancer, and diabetes better than Americans by an order of magnitude. And they spend one-fifth of what the US spends on health care.

My colleagues and I concluded that the secret lies partly in their strong faith community, in their deep social networks, and their habit of doing regular, low-intensity physical activity. They also benefited from a healthy daily dose of vitamin D from sunlight and extra calcium in the water. Diet also plays a big role.

**LE:** Like residents of other Blue Zones, people here eat a low-calorie, low-fat, plant-based diet. What foods are unique to the Nicoyan peninsula that Life Extension® readers can incorporate into their own diets?
DB: The big secret of the Nicoyan diet was the “three sisters” of Mesoamerican culture: beans, corn, and squash. A combination of beans and squash, eaten with corn tortillas, is rich in complex carbs, protein, calcium, and niacin. It naturally helps reduce bad cholesterol and increase good cholesterol. Nutritionist Leonardo Mata told me he thought the most significant component of the diet was how they prepared their corn [tortillas]. To prepare the dough, they soak whole corn kernels in calcium hydroxide—lime and water—which infuses the grain with **7.5 times** more calcium and unlocks certain amino acids otherwise unavailable in corn.

LE: What are some other foods eaten on the peninsula that contribute to a long life span?

DB: Squash—available in several varieties—provides high levels of useful carotenoids. Papayas grow like weeds in Nicoya, so people eat it, both green and ripe, almost every day. Its rich orange flesh contains vitamins A, C, and E, plus an enzyme called papain that counters inflammation. Yams have been a staple for the past century. Although these yams are similar in appearance, they are unrelated botanically to North American sweet potatoes. They are true yams, available in the US in produce markets serving Latin American communities. Their flesh is firm and white, even cooked, and they are a rich source of vitamin B6. Black beans, bananas, and pejivalles, or peach palms, round out their top longevity foods.

LE: What are peach palms and are they available in the US?

DB: A staple for Costa Rica, they are rarely seen for sale in the United States. One prominent Costa Rican researcher believes they may interact with a bacterium—*Helicobacter pylori*—that is closely associated with stomach cancer. Peach palms may explain why Nicoyans have the lowest rates of stomach cancer in Costa Rica.

LE: Thank you for sharing this important and useful information with our readers. I’m sure they’ve learned even more ways to increase the longevity and vitality of their own lives.

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

To order a copy of *The Blue Zones Solution*, call 1-800-544-4444 or visit LifeExtension.com

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Dan Buettner is an internationally recognized researcher, explorer, bestselling author, and National Geographic Fellow. His books include *The Blue Zones: Lessons for Living Longer From the People Who’ve Lived the Longest and Thrive: Finding Happiness the Blue Zones Way*. He founded Blue Zones®, a company that puts the world’s best practices in longevity and well-being into practice.

### SPICY BEAN BURGERS

Yields 4 burgers.

- 4 cups cooked and drained pinto beans or drained and rinsed canned pinto beans
- ¾ cup fresh whole-grain bread crumbs
- Up to 1 tablespoon bottled hot red pepper sauce, such as Tabasco®
- 2 teaspoons minced garlic
- ½ tablespoon Worcestershire sauce
- ½ teaspoon ground cumin
- ½ teaspoon salt
- Nonstick spray
- 4 whole-grain hamburger buns
- ¼ cup pico de gallo
- 4 small Romaine lettuce leaves
- 4 green bell pepper slices (optional)
- 4 thin red onion rings (optional)

1. Put the beans, bread crumbs, hot red pepper sauce, garlic, Worcestershire sauce, cumin, and salt in a large bowl. Use a potato masher to blend these ingredients into a smooth paste. Cover and refrigerate for 30 minutes to firm up.
2. Spray the grate of an outdoor gas grill with nonstick spray, cover, and heat to high. Or spray a large grill pan over medium-high heat for a few minutes until hot.
3. Meanwhile, use clean, wet hands to form the bean mixture into four even patties, each about 5 inches in diameter and ½-inch thick. Grill the patties until hot and a little crisp, about 6 minutes, turning once.
4. Place the patties on the bottom of the buns and top each with 2 tablespoons pico de gallo, as well as the lettuce and the tops of those buns. Garnish with pepper slices and onion rings as desired.
HOMEMADE GRANOLA
Yields 6 cups or 12 servings.

3 cups rolled oats (do not use quick-cooking or steel-cut oats)
½ cup chopped unsalted nuts, such as walnuts, pecans, and/or almonds
½ cup honey
¼ cup walnut oil, pecan oil, or olive oil
2 teaspoons vanilla extract
½ teaspoon ground cinnamon
½ teaspoon grated nutmeg
¼ teaspoon salt
½ cup dried berries or other chopped dried fruit, such as apples, pears, or pitted dates

1. Position the rack in the center of the oven and heat the oven to 350°F.
2. Mix the oats, nuts, honey, oil, vanilla, cinnamon, nutmeg, and salt in a large bowl until well combined. Spread onto a large-lipped baking sheet.
3. Bake for 10 minutes. Stir and continue baking until golden brown, about another 10 minutes. Place the baking sheet on a wire rack. Sprinkle the dried berries or fruit on top and stir well. Cool to room temperature, about an hour.

IKARIAN STEW
Yields 4 servings.

2 cups dried black-eyed peas
½ cup extra-virgin olive oil
1 large yellow or white onion, diced (about 1 ½ cups)
1 medium fennel bulb, trimmed, halved, and sliced into thin strips
2 teaspoons minced garlic
3 large carrots, peeled and chopped (about 1 cup)
1 large red globe, beefsteak, or heirloom tomato, diced (about ¾ cup)
2 tablespoons tomato paste
2 bay leaves
1 teaspoon salt
4 large kale leaves, slivered
½ cup chopped fresh dill

1. Spread the black-eyed peas on a large baking sheet and pick over to remove any damaged peas or debris. Put the peas in a large pot, add enough cool tap water to submerge by 2 inches, and bring to a boil over high heat. Boil for 1 minute. Set aside off the heat and soak for one hour. Drain in a colander set in the sink.

2. Warm ¼ cup oil in a large pot or Dutch oven set over medium heat. Add the onion and fennel; cook, stirring often, until soft, about 8 minutes. Add the garlic and cook until fragrant, about 20 seconds. Stir in the black-eyed peas, carrots, tomato, tomato paste, bay leaves, and salt until the tomato paste dissolves. Add enough water just to cover the vegetables. Raise the heat to medium-high and bring to a boil.

3. Cover, reduce the heat to low, and simmer slowly until the black-eyed peas are tender, about 50 minutes.

4. Stir in the kale leaves and dill. Cover and cook until the kale is tender, 5 to 10 minutes. Discard the bay leaves. Ladle into four bowls. Drizzle 1 tablespoon olive oil on top of each helping.
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- **Silicon**: Silicon is required for the formation of the protein cross-links that hold collagen and keratin molecules in their unique, functional shapes.7

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<td><strong>Retail Price</strong></td>
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References


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<td><strong>COMPREHENSIVE PANELS</strong></td>
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<td><strong>WEIGHT LOSS PANEL-COMPREHENSIVE</strong> (LC100028)</td>
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<td>Pregnenolone and Dihydrotestosterone (DHT) to provide an even more in-depth analysis of a man’s hormone status, Life Extension has created this panel as an addition to the Male Life Extension Panel. This panel provides valuable information about a testosterone metabolite that can affect the prostate, and the mother hormone that acts as a precursor to all other hormones.</td>
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<td><strong>FEMALE HORMONE ADD-ON PANEL</strong> <em>(LCADD)</em></td>
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<tr>
<td>Pregnenolone and Total Estrogens To provide an even more in-depth analysis of a woman’s hormone status, Life Extension has created this panel as an addition to the Female Life Extension Panel. This panel provides valuable information about total estrogen status, and the mother hormone that acts as a precursor to all other hormones.</td>
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**Note:** This CBC/Chemistry Profile is included in many Life Extension panels. Please check panel descriptions.
This test is packaged as a kit, requiring a finger stick performed at home.

This panel looks at vascular inflammatory biomarkers, Total and Free Testosterone, DHEA-S, Free T3, Free T4, and RBC Magnesium.

Metabolic as well as cardiovascular disease and the formation of vulnerable plaque. The panel contains the following tests: F2-Isoprostanes, Myeloperoxidase, and Oxidized LDL.

ANA screen, hs-CRP, TNF, Immunoglobulins, F2-Isoprostanes, Myeloperoxidase, and Oxidized LDL.

ANEMIA PANEL
CBC/Chemistry Profile (see description previous page), Ferritin, Total Iron Binding Capacity (TIBC), Vitamin B12, Folate, Insulin.

AUTOIMMUNE DISEASE SCREEN
ANA screen, hs-CRP, TNF, Immunoglobulins, IgA, IgG, IgM.

DIABETES MANAGEMENT PROFILE – COMPREHENSIVE

DIABETES MANAGEMENT PROFILE – BASIC
Hemoglobin A1C, Glucose, Insulin.

ADVANCED CARDIAC BIOMARKERS
ADVANCED OXIDIZED LDL PANEL
This panel looks at vascular inflammatory biomarkers, beginning with lifestyle choices to the development of metabolic as well as cardiovascular disease and the formation of vulnerable plaque. The panel contains the following tests: F2-Isoprostanes, Myeloperoxidase, and Oxidized LDL.

OXIDIZED LDL PANEL
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DHEA-S, Estradiol, Free and Total Testosterone, PSA

FEMALE BASIC HORMONE PANEL (LC100013)
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- Esophageal Guardian

**Energy Management**
- Adrenal Energy Formula
- Asian Energy Boost
- D-Ribose Powder
- D-Ribose Tablets
- Forskolin
- Mitochondrial Basics with BioPQQ®
- Mitochondrial Energy Optimizer with BioPQQ®
- NAD+ Cell Regenerator™
- Peak ATP® with GlycoCarn®
- POQ Caps with BioPQQ®
- Rhodiola Extract
- RiboGen™ French Oak Wood Extract
- Triple Action Thyroid

**Eye Health**
- Astaxanthin with Phospholipids
- Brie Eyes III
- Certified European Bilberry Extract
- Eye Pressure Support with Mirtogenol®
- MacuGuard® Oral Support
- MacuGuard® Oral Support with Astaxanthin
- Tear Support with MaquiBright®

**Fish Oil & Omegas**
- Mega EPA/DHA
- Mega GLA with Sesame Lignans
- OMEGA FOUNDATIONS™ Super Omega-3 EPA/DHA with Sesame Lignans & Olive Extract
- OMEGA FOUNDATIONS™ Super Omega-3 Plus EPA/DHA with Sesame Lignans, Olive Extract, Krill & Astaxanthin
- Organic Golden Flax Seed
- Proven® Purified Omega-7
- Vegetarian Sourced DHA

**Food**
- Rich Rewards® Breakfast Blend
- Rich Rewards® Breakfast Blend Natural Mocha Flavor
- Rich Rewards® Breakfast Blend Natural Vanilla Flavor
- Rich Rewards® Breakfast Blend Whole Bean Coffee
- Rich Rewards® Decaf Roast
- Stevia Sweetener

**Glucose Management**
- CinSulin® with InSea® and Crominex® 3+
- CoffeeGenc® Green Coffee Extract
- Mega Benfotamine
- Natural Glucose Absorption Control
- Tri Sugar Shield®

**Heart Health**
- Aspirin (Enteric Coated)
- Cardio Peak™ with Standardized Hawthorn and Arjuna
- Fibrogenic Resist™ with Nattokinase
- Folate & Vitamin B12 Caps
- Optimized Carnitine with GlycoCarn®
- Super Ubiquinol CoQ10
- Super Ubiquinol CoQ10 with BioPQQ®
- Super Ubiquinol CoQ10 with Enhanced Mitochondrial Support™
- Super-Absorbable CoQ10 Ubiquinone
- with d’Limonene
- TMG Powder
- TMG Liquid Capsules

**Hormone Balance**
- DHEA (Dehydroepiandrosterone)
- Inner Power
- Pregnenolone
- Triple Action Cruciferous Vegetable Extract with Resveratrol
- Triple Action Cruciferous Vegetable Extract

**Immune Support**
- AHCC®
- Echinacea Extract
- Enhanced Zinc Lozenges
- 26 Hyperimmunize Egg
- Immune Modulator with Tinofend®
- Immune Protect with PARACTIN®
- Immune Senescence Protection Formula™
- Kinoko® Gold AHCC
- Kyolic® Garlic Formula 102
- Kyolic® Garlic Formula 105
- Kyolic® Reserve
- Lactoferin (apolactoferin) Caps
- NK Cell Activator™
- Optimized Garlic
- Optimized Quercetin
- Peony Immune
- ProBoost Thymic Protein A
- Reishi Extract Mushroom Complex
- Standardized Cistanche Ten Mushroom Formula®
- Zinc Lozenges

**Inflammation Management**
- 5-LOX Inhibitor with AprèsFlex®
- Advanced Bio-Curcumin® with Ginger & Turmerones
- Black Cumin Seed Oil with Bio-Curcumin®
- Black Cumin Seed Oil
- Boswellia
- Cytokine Supress™ with EGCG
- Nervia®
- Serrafflazyme
- Specially-Coated Bromelain
- Super Bio-Curcumin®
- Zyflamend® Whole Body

**Joint Support**
- Arthro-Immune Joint Support
- ArthroMax® Advanced with UC-II® & AprèsFlex®
- ArthroMax® with Theaflavins & AprèsFlex®
- Bio-Collagen with Patented UC-II®
- Fast-Acting Joint Formula
- Glucosamine/Chondroitin Capsules
- Krill Healthy Joint Formula
- MSM (Methylsulfonylmethane)

**Kidney & Bladder Support**
- Cran-Max® Cranberry Whole Fruit Concentrate
- Optimized Cran-Max® with Ellirose™
- Water-Soluble Pumpkin Seed Extract

**Liver Health & Detoxification**
- Anti-Alcohol Antioxidants with HepatoProtection Complex
- Calcium D-Gluconate
- Chlorella
- Chlorophyll
- European Milk Thistle
- Glutathione, Cysteine & C
- HepatoPro
- Liver Efficiency Formula
- Mega L-Glutathione Capsules
- N-Acetyl-L-Cysteine
- PectaSol-C®
- Pyrularin
- Silymarin
- i26 Hyperimmune Egg
- Immune Modulator with Tinofend®
- Immune Protect with PARACTIN®
- Immune Senescence Protection Formula™
- Kinoko® Gold AHCC
- Kyolic® Garlic Formula 102
- Kyolic® Garlic Formula 105
- Kyolic® Reserve
- Lactoferin (apolactoferin) Caps
- NK Cell Activator™
- Optimized Garlic
- Optimized Quercetin
- Peony Immune
- ProBoost Thymic Protein A
- Reishi Extract Mushroom Complex
- Standardized Cistanche Ten Mushroom Formula®
- Zinc Lozenges

**Longevity & Wellness**
- AMPK Activator
- AppleWise Polyphenol Extract
- Berry Complete
- Blueberry Extract
- Blueberry Extract with Pomegranate
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<td>Glycine</td>
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<td>Melatonin</td>
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<td>Optimized Tryptophan Plus</td>
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| **Sports Performance** |
| Creatine Capsules |
| Creatine Whey Glutamine Powder (Vanilla Flavor) |
| DMG (N,N-dimethylglycine) |
| New Zealand Whey Protein Concentrate, (Natural Chocolate and Vanilla Flavor) |
| Pure Plant Protein |
| Tart Cherry Extract |
| Whey Protein Isolate |
| (Chocolate and Vanilla Flavor) |

| **Vitamins** |
| Ascorbyl Palmitate |
| Benfotiamine with Thiamine |
| Beta-Carotene |
| BioActive Complete B-Complex |
| Biotin |
| Buffered Vitamin C Powder |
| Daily C+ |
| Fast-C+ with Dihydroquercetin |
| Gamma E Tocopherol with Sesame Lignans |
| Gamma E Tocopherol/Tocotrienols |
| High Potency Optimized Folate |
| Inositol Caps |
| Liquid Emulsified Vitamin D3 |
| Liquid Vitamin D3 |
| Low-Dose Vitamin K2 |
| Methylcobalamin |
| MK-7 |
| Natural Vitamin E |
| No Flush Niacin |
| Optimized Folate (L-Methylfolate) |
| Pantothenic Acid (Vitamin B-5) |
| Pyridoxal 5’-Phosphate Caps |
| Super Absorbable Tocotrienols |
| Super Ascorbate C Capsules |
| Super Ascorbate C Powder |
| Super K with Advanced K2 Complex |
| Vitamin B12 |
| Vitamin B6 |
| Vitamin C with Dihydroquercetin |
| Vitamin D3 with Sea-Iodine™ |
| Vitamin D3 |
| Vitamins D and K with Sea-Iodine™ |

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

| **Men's Health** |
| Mega Lycopene Extract |
| PalmettoGuard® Saw Palmetto with Beta-Sitosterol |
| PalmettoGuard® Saw Palmetto/Nettle Root Formula with Beta-Sitosterol |
| Pomi-T™ |
| PrenoPure™ Natural Sex for Men |
| Super MiraForte with Standardized Lignans |
| Triple Strength ProstaPollen™ Ultra Natural Prostate |

| **Minerals** |
| Boron |
| Chromium Ultra |
| Copper |
| Iron Protein Plus |
| Magnesium (Citrate) |
| Magnesium Caps |
| Only Trace Minerals |
| Optimized Chromium with Cromines® 3+ Sea-Iodine™ |
| Se-Methyl L-Selenocysteine |
| Super Selenium Complex |
| Vanadyl Sulfate |
| Zinc Caps |

| **Miscellaneous** |
| Advanced Iodine Complete Solarshield® Sunglasses |

| **Mood & Stress Management** |
| 5 HTP |
| L-Theanine |
| Natural Stress Relief |
| SAAme (S-Adenosyl-Methionine) |

| **Multivitamins** |
| Children’s Formula Life Extension Mix™ |
| Comprehensive Nutrient Packs ADVANCED Life Extension Mix™ Capsules without Copper |
| Life Extension Mix™ Capsules |
| Life Extension Mix™ Powder without Copper |
| Life Extension Mix™ Powder |
| Life Extension Mix™ Tablets with Extra Niacin |
| Life Extension Mix™ Tablets without Copper |
| Life Extension Mix™ Tablets |
| Once-Daily Health Booster |
| One-Per-Day Tablets |
| Two-Per-Day Capsules |
| Two-Per-Day Tablets |

| **Personal Care** |
| Anti-Aging Rejuvenating Scalp Serum Biosil |
| Dr. Proctor’s Advanced Hair Formula Biosil |
| Dr. Proctor’s Shampoo European Leg Solution Featuring Certified Diosmin 95 |
| Face Master Platinum Facial Toning System |
| Hair, Skin & Nails Rejuvenation Formula w/VERISOL™ |

| **Skin Care** |
| Advanced Anti-Glycation Peptide Serum |
| Advanced Lightening Cream |
| Advanced Hand Therapy |
| Advanced Triple Peptide Serum |
| Advanced Under Eye Serum with Stem Cells |
| Amber Self MicroDermAbrasion |
| Anti-Aging Face Oil |
| Anti-Aging Mask |
| Anti-Aging Rejuvenating Face Cream |
| Anti-Glycation Serum with Blueberry & Pomegranate Extracts |
| Antioxidant Facial Mist |
| Anti-Oxidant Rejuvenating Foot Cream |
| Anti-Oxidant Rejuvenating Foot Scrub |
| Anti-Oxidant Rejuvenating Hand Cream |
| Anti-Redness & Adult Blemish Lotion |
| Bioflavonoid Cream |
| Broccoli Sprout Cream |
| Collagen Boosting Peptide Serum |
| Corrective Clearing Mask |
| DNA Repair Cream |
| Dual-Action MicroDermAbrasion |
| Enhanced FernBlock® with Red Orange Complex |
| Essential Plant Lipids Reparative Serum |
| Face Rejuvenating Anti-Oxidant Cream |
| Fine Line-Less |
| Healing Formula |
| Healing Mask |
| Healing Vitamin K Cream |
| Hyaluronic Facial Moisturizer |
| Hyaluronic Oil-Free Facial Moisturizer |
| Hydrating Anti-Oxidant Facial Mist |
| Hydroderm |
| Lifting & Tightening Complex |
| Lycopene Cream |
| Melatonin Cream |
| Mild Facial Cleanser |
| Multi Stem Cell Tightening Complex |
| Neck Rejuvenating Anti-Oxidant Cream |
| Pigment Correcting Cream |
| Rejuvenex® Body Lotion |
| Rejuvenex® Factor Firming Serum |
| Renewing Eye Cream |
| Resveratrol Anti-Oxidant Serum |
| Skin Lightening Serum |
| Skin Restoring Phytoceramides with Lipowheat® |
| Skin Stem Cell Serum |
| Stem Cell Cream with Alpine Rose |
| Tightening & Firming Neck Cream |
| Ultra Lip Plumper |
| Ultra Rejuvenex® |
| Ultra Rejuvenight® |
| Ultra Wrinkle Relaxer |
| Under Eye Refining Serum |
| Under Eye Rescue Cream |
| Vitamin C Serum |
| Vitamin D Lotion |
| Vitamin E-essential Cream |
| Youth Serum |

| **Probiotics** |
| Bifido GI Balance BroccoliMax® FlorAssist® Heart Health Probiotic FlorAssist® Oral Hygiene FlorAssist® Balance FlorAssist® Throat Health Jarro-Dophilus EPS® Theracle® Probiotics TruFlora® Probiotics |

| **Hair Care** |
| Hair Suppression Formula |
| Life Extension Toothpaste |
| Sinus Cleanser |
| Venotone |
| Xylitol Mouthwash |

| **Cat Mix** |
| Dog Mix |

| **Pet Care** |
| **Probiotics** |
| Bifido GI Balance BroccoliMax® FlorAssist® Heart Health Probiotic FlorAssist® Oral Hygiene FlorAssist® Balance FlorAssist® Throat Health Jarro-Dophilus EPS® Theracle® Probiotics TruFlora® Probiotics |

| **Hair, Skin & Nail Care** |
| Anti-Aging Rejuvenating Scalp Serum Biosil Dr. Proctor’s Advanced Hair Formula Dr. Proctor’s Shampoo European Leg Solution Featuring Certified Diosmin 95 Face Master Platinum Facial Toning System Hair, Skin & Nails Rejuvenation Formula w/VERISOL™ |

| **Supplements** |
| **Sleep** |
| Bioactive Milk Peptides |
| Enhanced Natural Sleep with Melatonin |
| Enhanced Natural Sleep without Melatonin |
| Fast-Acting Liquid Melatonin |
| Glycine |
| L-Tryptophan |
| Melatonin |
| Optimized Tryptophan Plus |

| **Sports Performance** |
| Creatine Capsules |
| Creatine Whey Glutamine Powder (Vanilla Flavor) |
| DMG (N,N-dimethylglycine) |
| New Zealand Whey Protein Concentrate, (Natural Chocolate and Vanilla Flavor) |
| Pure Plant Protein |
| Tart Cherry Extract |
| Whey Protein Isolate |
| (Chocolate and Vanilla Flavor) |

| **Vitamins** |
| Ascorbyl Palmitate |
| Benfotiamine with Thiamine |
| Beta-Carotene |
| BioActive Complete B-Complex |
| Biotin |
| Buffered Vitamin C Powder |
| Daily C+ |
| Fast-C+ with Dihydroquercetin |
| Gamma E Tocopherol with Sesame Lignans |
| Gamma E Tocopherol/Tocotrienols |
| High Potency Optimized Folate |
| Inositol Caps |
| Liquid Emulsified Vitamin D3 |
| Liquid Vitamin D3 |
| Low-Dose Vitamin K2 |
| Methylcobalamin |
| MK-7 |
| Natural Vitamin E |
| No Flush Niacin |
| Optimized Folate (L-Methylfolate) |
| Pantothenic Acid (Vitamin B-5) |
| Pyridoxal 5’-Phosphate Caps |
| Super Absorbable Tocotrienols |
| Super Ascorbate C Capsules |
| Super Ascorbate C Powder |
| Super K with Advanced K2 Complex |
| Vitamin B12 |
| Vitamin B6 |
| Vitamin C with Dihydroquercetin |
| Vitamin D3 with Sea-Iodine™ |
| Vitamin D3 |
| Vitamins D and K with Sea-Iodine™ |

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

| **Women's Health** |
| Advanced Natural Sex for Women® 50+ |
| Breast Health Formula |
| Femmenessence MacaPause® |
| Natural Estrogen without Soy Isoflavones |
| Natural Estrogen |
| ProgestaCare® for Women |
| Super-Absorbable Soy Isoflavones |
| Ultra Soy Extract |
## A

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Product</th>
<th>Retail Each</th>
<th>1 Unit Each</th>
<th>4 Unit Each</th>
<th>10 Unit Each</th>
<th>GTY Total</th>
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<td>ASHWAGANDHA EXTRACT (Optimized) • 60 veg. caps</td>
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**SUBTOTAL OF COLUMN 3**

**SUBTOTAL OF COLUMN 4**

**Deduct an additional 10% on all products during Super Sale!**
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<th>1 Unit Each</th>
<th>4 Unit Each</th>
<th>10 Unit Each</th>
<th>Your Price</th>
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**SUPER SALE SAVINGS ON ALL PRODUCTS**

**TO ORDER CALL: 1.954.766.8433 or 1.800.544.4440 ■ TO ORDER ONLINE VISIT: www.LifeExtension.com/SuperSale**

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

**JANUARY 2016**

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

**OFFER ENDS FEBRUARY 1, 2016**

**TO ORDER CALL: 1.954.766.8433 or 1.800.544.4440 ■ TO ORDER ONLINE VISIT: www.LifeExtension.com/SuperSale**

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**SUBTOTAL OF COLUMN 7**

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**SUBTOTAL OF COLUMN 8**

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

**JANUARY 2016**
TO ORDER CALL: 1.954.766.8433 or 1.800.544.4440 ■ TO ORDER ONLINE VISIT: www.LifeExtension.com/SuperSale

**SUPER SALE SAVINGS ON ALL PRODUCTS**

DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE

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<td>Red Yeast Rice (Bluebonnet) • 600 mg, 60 veg. caps</td>
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**SUBTOTAL OF COLUMN 9**

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

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**Not sure exactly which supplements you need?**

Talk to a Health Advisor toll-free at 1-800-226-2370
ORDER SUBTOTALS

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Please mail to: Life Extension, P.O. Box 407198 • Ft. Lauderdale, Florida 33340-7198, or call toll free 1-800-544-4440 • Fax: 866-728-1050

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Prices subject to change without notice. Please notify Life Extension of any address change.

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INTRODUCING YOUR HEALTHY REWARDS—Because You Deserve More

Introducing Your Healthy Rewards—the exciting new program exclusively for Life Extension customers. Your Healthy Rewards earns you 2% LE Dollars back on every purchase you make*...and the best part is, Your Healthy Rewards is FREE—no membership involved, no commitment required. The reason behind Your Healthy Rewards is simple: we believe that you deserve more. (Current Life Extension members earn 4%.)

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www.LifeExtension.com/Rewards

* You earn LE Dollars on all your Life Extension purchases (except shipping fees, CHOICE and Premier program fees, Life Extension Magazine® subscriptions, or any purchases made with LE Dollars or gift card). Redeem LE Dollars for any purchase such as products, labs, sale items, and shipping fees at the rate of 1 LE Dollar being equal to $1 U.S Dollar at checkout. LE Dollars may not be redeemed for Premier program fees, CHOICE program fees, Life Extension Magazine® subscriptions, or to purchase Gift Cards. LE Dollars have no cash value and are not redeemable for cash, transferable, or assignable for any reason.

† CHOICE Standard pre-paid shipping offers unlimited shipping to any mailing address within the 50 U.S. states, excluding U.S. territories. CHOICE also gives you discounts on non-standard shipping, shipping outside of the United States, and expedited shipping costs. CHOICE pre-paid unlimited shipping excludes blood test products and gift cards. This offer is not available to international customers serviced by distributors of Life Extension products.
Maintaining optimal vitamin B status becomes critical as we age. Not only are B vitamins required to support normal metabolic function, but they also support healthy homocysteine levels and help facilitate cognitive function. B vitamins must be replenished daily because they are water soluble and easily depleted from the body. Stress, alcoholic beverages, and some medications can also quickly deplete B vitamins.

**Enzymatically Active B Vitamins**

When conventional B vitamins are ingested, they must be enzymatically converted in the body to metabolically active forms. The new BioActive Complete B-Complex provides enzymatically active forms of meaningful potencies of each B vitamin. This includes the pyridoxal 5'-phosphate form of vitamin B6 (the metabolically active form, shown to protect lipids and proteins against glycation reactions) and the most biologically active form of folate called 5-methyltetrahydrofolate (5-MTHF).

**5-MTHF** is up to 7 times more bioavailable than folic acid and requires no enzymatic conversion to become metabolically active. Studies show 5-MTHF achieves optimal blood levels of active folate—and more importantly, supports healthy homocysteine levels in those within the normal range, while promoting survival in human study subjects. And unlike folic acid, 5-MTHF can cross the blood-brain barrier to facilitate cognitive function.

The meaningful potencies and enzymatically active vitamins in BioActive Complete B-Complex deliver a full spectrum of key effects that most commercial B-complex supplements do not.

To order **BioActive Complete B-Complex**, call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com).
It's not easy to get all the vital nutrients you need to take care of your eyes from food alone. Fortunately, MacuGuard® Ocular Support with Astaxanthin contains the nutritional building blocks necessary to maintain the structural integrity of your eyes.

MacuGuard® Ocular Support with Astaxanthin maintains eye health in many ways: 1-7

- Supports lutein concentration in the eye
- Supports efficient absorption of lutein in the bloodstream
- Provides phospholipids to enhance lutein in the cell membrane
- Maintains zeaxanthin concentrations in the eye
- Provides meso-zeaxanthin, which is difficult to obtain from dietary sources
- Contains cyanidin-3-glucoside, shown to help with night vision.
- Provides astaxanthin to protect against free radical-induced DNA damage, which may play a protective role against eye fatigue.

Contains soybeans.
LuteinPlus® and Mz® are registered trademarks of Nutriproducts Ltd., UK, licensed under U.S. Patent 8,623,428.

To order MacuGuard® Ocular Support with Astaxanthin, call 1-800-544-4440 or visit www.LifeExtension.com

References
Zinc stimulates the activity of about 300 enzymes¹ and fortifies the immune system.²

Taking the best zinc lozenge is important for maintaining the body’s natural defense system during the cold season—and throughout the year.

Enhanced Zinc Lozenges is a special “ionic formula” that delivers on the original promise of seasonal immune support.

IMMUNE SUPPORT FOR SEASONAL CHANGES

Scientific evidence is accumulating that zinc acetate is the preferred zinc compound to provide enhanced seasonal immune support.

Zinc acetate releases 100% of its zinc as ionic zinc—positively charged zinc ions. Zinc acetate lozenges have been shown to strongly support immune function.³⁻⁵

Life Extension® Enhanced Zinc Lozenges provide zinc acetate with no other ingredients that could reduce the delivery of these immune-supportive, positively charged zinc ions. Enhanced Zinc Lozenges come in a naturally flavored peppermint lozenge.

SUGGESTED USE

The suggested serving size of one vegetarian lozenge of Life Extension® Enhanced Zinc Lozenges provides:

| ZINC (zinc acetate) | 18.75 mg |

These special zinc lozenges are not meant for daily use. Only a few of these lozenges are usually required when extra support is needed for seasonal changes. Its good to keep a bottle close by at home or work for immediate access.

References

Fat-Soluble Nutrients Missing From Most Multi-Vitamin Formulas

Life Extension®’s Health Booster is a cost-effective formula that combines a variety of valuable nutrients in just one softgel. Once-Daily Health Booster provides the following nutrients:

**Vitamin K1** is found in plants. It is often bound to plant fiber and requires intestinal conversion to transform into bioactive vitamin K2. Data supports value of K1 in addition to the K2 forms. 1, 2

**Vitamin K2** is the active form that keeps calcium in bone and out of arteries. MK-4 is rapidly absorbed, 3, 4 while MK-7 provides 24-hour bioavailability of vitamin K2. 5

**Sesame lignans** increases tissue levels of gamma tocopherol, which plays a pivotal role in quenching certain kinds of inflammation. 6

**Lycopene** supports prostate health, protect against free radical activity, and guard against LDL oxidation. 7, 8

**Chlorophyllin** offers protection against environmentally induced DNA damage from toxins like smoke, emission particles, and foods cooked at high temperatures. 9

**Black currant extract** (C3G) anthocyanins promotes eye health and help ease eye fatigue. 10

**Vitamin B12** helps maintain a healthy nervous system and metabolism. 11 Vitamin B12 levels decrease with age. 12

**Trans-zeaxanthin**, **meso-zeaxanthin**, and lutein supports eye health and healthy vision. 13

**Gamma tocopherol** is a form of vitamin E that quenches the damaging peroxynitrite free radical. 14, 15 Those who take alpha-tocopherol should also take gamma tocopherol.

**Blueberry extract** boosts DNA function and sustain healthy blood sugar levels already within normal range. 16

**Gamma tocopherol** is a form of vitamin E that supports value of K1 in addition to the K2 forms. 17, 18

**Beta tocopherol < 1.9 mg**

**Delta tocopherol = 70.4 mg**

**Gamma tocopherol = 1.9 mg**

**Gamma E Mixed Tocopherols = 70.4 mg**

**Chlorophyllin** supports eye health and help ease eye fatigue. 19

**MacuGuard® Carotenoid Phospholipid Blend**

- **Phospholipids**, marigold extract (flower) [providing 10 mg free lutein, 4 mg meso-zeaxanthin & trans-zeaxanthin]
- **C3G** (Cyanidin-3-glucoside) [from European black currant extract (fruit)]
- **Lycopene proprietary blend** [from Micronized Lycopene and Tomat-O-Red® natural tomato extract (fruit)]
- **Sesame Seed Lignan Extract**
- **Wild Blueberry Whole Extract** (fruit)

Each Bottle Of Health Booster Lasts Two Months

**Super Cost Effective!**

Just one softgel of the new Health Booster taken with a meal provides optimized potencies of fat-soluble vitamins, carotenoids, and other plant extracts. If these nutrients were taken separately, one would have to swallow many capsules and spend 2-3 times more money.

To order Once-Daily Health Booster, call 1-800-544-4440 or visit www.LifeExtension.com

**Once-Daily Health Booster**

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**One daily Health Booster softgel provides:**

- **Vitamin K1** 1,500 mcg
- **Vitamin K2 (MK-4)** 1,000 mcg
- **Vitamin K2 (MK-7)** 200 mcg
- **Vitamin B12** 300 mcg
- **Chlorophyllin** 100 mg
- **Gamma E Mixed Tocopherols** 359 mg
  - Gamma tocopherol 197.45 - 269.25 mg
  - Delta tocopherol 71.8 - 107.7 mg
  - Alpha tocopherol 30.52 - 43.08 mg
  - Beta tocopherol < 17.95 mg

**Lycopene proprietary blend**

- **Tomato extract (fruit)**

**Sesame lignans** increases tissue levels of gamma tocopherol, which plays a pivotal role in quenching certain kinds of inflammation. 6

**Black currant extract** (C3G) anthocyanins promotes eye health and help ease eye fatigue. 10

**Vitamin B12** helps maintain a healthy nervous system and metabolism. 11 Vitamin B12 levels decrease with age. 12

**References**


Caution: If taking anticoagulant or antiplatelet medication, consult your healthcare provider before taking this product.

**Tomat-O-Red®** is a registered trademark of Lycotec, LTD. LuteinPlus® and 1Mz® are registered trademarks of NutriProducts Ltd., UK, licensed under U.S. Patent 8,623,428.
Are You Getting the Maximum Potency from Your Daily Vitamin?

Life Extension®’s Two-Per-Day formulas are the highest-potency multivitamins on the market. In fact, they have the highest potencies of any science-based multivitamin formula that can fit inside two easy-to-take tablets or capsules.

Compared to Centrum® (the leading multivitamin), Two-Per-Day provides:

- 50 times more vitamin B1
- 12 times more vitamin B12
- 25 times more vitamin B6
- 10 times more biotin
- 10 times more selenium
- 8 times more vitamin C
- 2 times more vitamin D
- 2 times as much vitamin E
- 2.5 times as much vitamin B3
- 3 times as much zinc

Life Extension®’s Two-Per-Day contains 5-methyltetrahydrofolate (5-MTHF), the active form of folate that is up to 7 times more bioavailable than folic acid. This greater bioavailability is especially important in people with a genetic enzyme deficiency since it requires no conversion to become metabolically active.

### Two-Per-Day Tablets

Item #02015 • 120 tablets (2 month supply)

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<tbody>
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<td>1 bottle</td>
<td>$20</td>
</tr>
<tr>
<td>4 bottles</td>
<td>$13.50 each</td>
</tr>
</tbody>
</table>

For the complete list of ingredients, trademarks, cautions, references, dosage and use, please visit www.LifeExtension.com.

*Two-Per-Day provides a small amount of gamma tocopherols as part of natural mixed tocopherols, which include natural vitamin E.

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52 REBUTTAL TO MEDIA ATTACK AGAINST VITAMIN D
The American Medical Association published a deeply flawed report against vitamin D based on skewed data. Dr. Ward Dean writes a scathing rebuttal to this spurious attack on one of the better-documented disease-preventing nutrients.

70 SUPPRESS AFTER-MEAL SURGES OF GLUCOSE AND DEADLY FATS
With millions of Americans at risk for metabolic disorders, scientists have identified a fiber that selectively blocks absorption of harmful fats in the bloodstream and limits after-meal glucose spikes.

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Researchers have discovered a targeted probiotic that reduces indicators of plaque buildup, gingivitis, bleeding gums, and pocket depth between gums and tooth roots.

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Three natural compounds have been shown to ward off immune senescence and reverse harmful immune cell imbalances that accelerate systemic aging.

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New studies confirm that people with higher blood levels of vitamin D have sharply lower rates of stroke-induced paralysis and death in the hospital as well as fewer psychiatric disorders and a lower risk of multiple sclerosis.

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