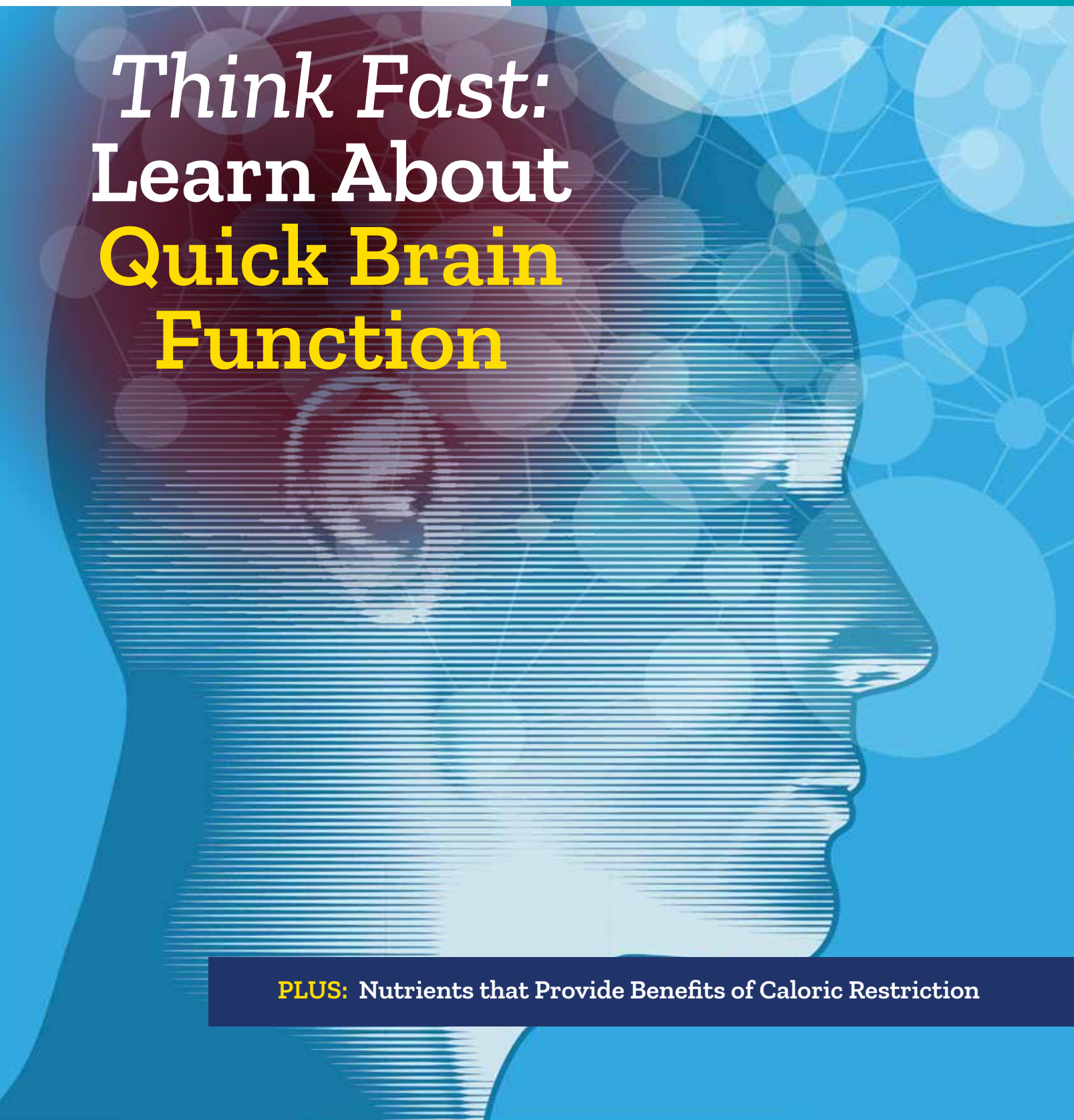
LIFE EXTENSION®
The Science of a Healthier Life™
September/October 2020

FEATURE ARTICLES

Think Fast: Learn About Quick Brain Function



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References

1. *Immun Ageing*. 2009 Jun 12;6:9.
2. https://www.sciencedirect.com/science/article/abs/pii/S1756464618303621.
3. *Am J Clin Nutr*. 2004 Mar;79(3):444-50.
4. *J Trace Elem Med Biol*. 2010 Apr;24(2)89-94.

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Melatonin 3 mg
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Item #00332

Melatonin 6 Hour Timed Release 750 mcg
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Item #01788

Melatonin 6 Hour Timed Release 3 mg
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Item #01786

Melatonin 1 mg
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Enhanced Sleep with Melatonin
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LIFE EXTENSION®

The Science of a Healthier Life®

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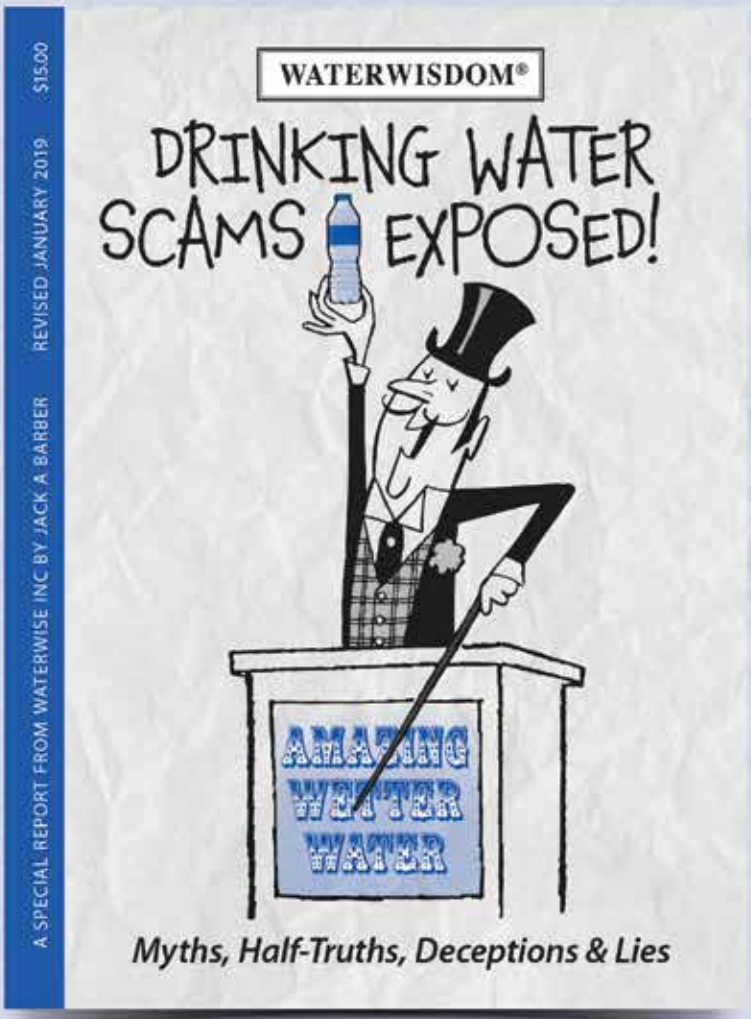

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September/October 2020

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IN THE NEWS

HEALTHY EATING

MEDICAL ADVISORY BOARD

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 publicationzs and served as an editor for the Journal of Medicinal Food.

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

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

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

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

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In the News

Vitamin C Could Lower Ventilation Duration

Results of an analysis published in the *Journal of Intensive Care* revealed an association between the administration of **vitamin C** to critically ill patients and a reduction in the length of time that the use of a ventilator was required.*

Researchers pooled the results of eight controlled trials that compared the length of ventilation among patients who received intravenous or orally administered vitamin C, to the ventilation duration of control groups who did not receive the vitamin.

Upon having determined a **14%** reduction in time spent using a ventilator among subjects who received vitamin C infusions, they subsequently limited the analysis to five trials that involved longer ventilation times of 10 hours or more, which suggests more severe disease.

The results in these critically ill patients found an average reduction in **ventilator** time of **25%** among patients who received **1-6 grams** of intravenous or oral **vitamin C** per day.

Editor's Note: The authors concluded that, "Given the strong evidence of benefit for more severely ill critical care patients along with the evidence of very low vitamin C levels in such patients, ICU patients may benefit from the administration of vitamin C. Further studies are needed to determine optimal protocols for its administration."

* *J Intensive Care.* 2020 Feb 7;8:15.

Supplementing with Glucosamine Linked with Reduced Risk of Type II Diabetes

A report published in the American Diabetes Association journal *Diabetes Care* revealed a significant association between the use of **glucosamine** and a *lower* risk of developing type II diabetes.*

The study included 404,508 men and women enrolled in UK Biobank, a population-based prospective study that was established to facilitate investigations of genetic and nongenetic determinants of diseases of middle and older age.

Questionnaires completed upon enrollment in UK Biobank reported the regular use of various supplements, while blood samples collected at the time provided information concerning levels of C-reactive protein.

Participants were free of cancer, cardiovascular disease and diabetes at the beginning of the study. Type II diabetes was diagnosed among 7,228 subjects during a median follow-up of 8.1 years. Glucosamine supplementation in men and women was associated with a **17%** lower risk of developing diabetes during follow-up.

Editor's Note: C-reactive protein levels at the beginning of the study were significantly lower in glucosamine users than nonusers. Among participants whose blood levels of CRP placed them among the top **25%** of subjects, the use of glucosamine was associated with an **18.8%** lower risk of diabetes compared to nonusers. Glucosamine has long been used by people with cartilage degenerative disorders in their joints.

* *Diabetes Care.* 2020 Jan 27.

Iron Interferes with the Benefits of Lycopene

Lycopene is a carotenoid found in tomatoes and other red fruits that gives them their bright color. It also provides numerous health benefits and has been associated with a lower risk of prostate[1] and lung[2] cancers.

Unfortunately, those benefits could be reduced if tomatoes are consumed with iron-rich foods, like meat.

According to a recent study published in *Molecular Nutrition & Food Research*, iron interferes with the body's ability to absorb lycopene.[3]

For this study, researchers had a small group of people consume a tomato-extract-based shake, either with or without iron.

Numerous blood draws and digestive samples revealed that lycopene levels in the blood and in the stomach were significantly **lower** when lycopene was consumed with iron.

"When people had iron with their meal, we saw almost a *two-fold drop* in lycopene uptake over time," said the study's lead author, Dr. Rachel Kopec.

This means that less lycopene is available for the body to utilize.

Editor's Note: This study highlights why iron is **not** included in **Life Extension®** supplements. Those with low iron levels should supplement with **iron** at a different time of the day from when they take **lycopene**. Note that **calcium** and **green tea** block iron absorption. It is best to take iron with **vitamin C**, which enhances iron absorption.

References

1. *Exp Biol Med (Maywood).* 2002 Nov; 227(10):852-9.
2. *Am J Clin Nutr.* 2000 Oct;72(4):990-7.
3. *Mol Nutr Food Res*. 2019 Nov;63(22): e1900644.

Specific Nutrients May Improve the Body's Immune Response to RNA Viruses

An article published in *Progress in Cardiovascular Diseases* proposes the use of nutritional supplements to enhance the body's **type 1 interferon immune response** to influenza and coronaviruses. These viruses have **RNA**, rather than **DNA**, as their genetic material.*

"Activation of toll-like receptor 7 (TLR7) by single-stranded viral RNA trapped within endosomes provides a key stimulus to type 1 interferon induction by RNA viruses," authors Mark F. McCarty and James J. DiNicolantonio wrote.

Based on this and other research findings, the researchers identified the antioxidant compounds **lipoic acid**, **ferulic acid** and **sulforaphane** as nutrients that may enhance TLR7-mediated induction of type 1 interferon.

Spirulina or a protein in spirulina extracts known as phycocyanobilin may also improve this response to RNA viruses.

N-acetylcysteine (NAC) increases the production of glutathione and could help protect TLR7 from damage due to oxidation.

The provisional daily dosage suggestions for nutraceuticals that might aid control of RNA viruses including influenza and coronavirus were as follows:

Ferulic acid	500 mg-1,000 mg
Lipoic acid	1,200 mg-1,800 mg (in place of ferulic acid)
Spirulina	15 grams (or 100 mg of phycocyanobilin or PCB)
N-Acetylcysteine	1,200 mg–1,800 mg
Selenium	50 mcg-100 mcg
Glucosamine	3,000 mg or more
Zinc	30 mg-50 mg
Yeast Beta-Glucan	250 mg-500 mg
Elderberry	600 mg–1,500 mg

In an interview, Dr. DiNicolantonio told *Thailand Medical News*, "Therefore, it is clear that certain **nutraceuticals** have antiviral effects in both human and animal studies. Considering that there is no treatment for the new **coronavirus**…we welcome further studies to test these **nutraceuticals** as a strategy to help provide relief in those infected with encapsulated RNA viruses."

Editor's Note: Another mechanism of type 1 interferon response, activation of mitochondrial antiviral-signaling protein (MAVS), can be upregulated by a high dose of **glucosamine**.

* *Prog Cardiovasc Dis*. 2020 Feb 12.

Supplementation with Vitamin C Associated with Boost to Immunity

A randomized, double-blind trial reported in *BMJ Military Health* showed that daily vitamin C supplementation resulted in a lower risk of contracting the common cold.*

In their discussion of the findings, the researchers remarked that vitamin C boosts immunity by improving white blood cell function against viruses. It also has an antihistamine action that helps reduce cold symptoms.

The trial included 1,444 men. For a period of 30 days, 695 participants received **2,000 mg** of vitamin C three times per day. The other individuals were given a placebo.

The subjects supplemented with vitamin C were less likely to catch a cold compared to the placebo group.

The protective effect of vitamin C was found to be stronger among those who had never smoked.

Editor's Note: The study participants were enlisted military members in the army of South Korea, whose average age was 21.7 years.

* *BMJ Mil Health*. 2020 Mar 5;bmjmilitary- 2019-001384.

Vitamin K Deficiency Associated with Harmful Calcium Accumulation

Vitamin K deficiency plays a role in the development of a disease called calciphylaxis, according to a study published in the *Journal of the American Society of Nephrology*.[1]

In **calciphylaxis**, calcium accumulates in the small blood vessels of fat and skin tissues. It occurs mainly in patients on dialysis, and can cause blood clots, skin ulcers, skin infections, and ultimately, death.

In a study that included 20 hemodialysis patients with calciphylaxis and 20 without it, researchers found that people with the disease had higher plasma levels of ***inactive*** **matrix Gla protein** (MGP).

MGP is a potent inhibitor of vascular **calcification**, but in order to work properly, MGP needs to be *activated* by an enzyme that requires **vitamin K**.

The researchers found that patients with calciphylaxis had a lower concentration of activated MGP. In fact, for each **0.1 unit reduction** in relative active MGP concentration, there was a more than **2-fold** increase in calciphylaxis risk.

They also found that vitamin K deficiency was associated with a lower concentration of activated GMP.

This study indicates that adequate vitamin K is essential for processes that help prevent calciphylaxis in people on dialysis.

Editor's Note: In a separate study, researchers found that vitamin K showed promise for treating calciphylaxis.[2]

References

1. *J Am Soc Nephrol.* 2017 Jun;28(6):1717-22.
2. Available at: https://www.renalandurologynews.com/home/conference-highlights/kidney-week-annual-meeting/kidney-week-2019/vitamin-k-shows-promise-for-calciphylaxis/. Accessed April 22, 2020.

Connection Between Gum Disease and Alzheimer's Disease Confirmed

A study published in the *Journal of Clinical Investigation* was the first to connect the presence of the gingivitis pathogen *Porphyromonas gingivalis* in the brain to factors associated with Alzheimer's disease.*

Previously, numerous studies had shown that periodontitis (gum disease) is closely associated with cognitive impairment and Alzheimer's disease.

And studies done **post-mortem** had found that the periodontal pathogen *Porphyromonas gingivalis* is present in the brains of Alzheimer's patients.

In the more recent study, researchers induced experimental gingivitis in mice by giving them repeated oral doses of *Porphyromonas gingivalis* for 22 weeks. Another group of mice served as a control group.

Testing revealed that in the mice that received *Porphyromonas gingivalis*, the pathogen was present in the brain tissue in the hippocampus (the area of the brain that plays a major role in learning and memory).

In addition, the study showed that the presence of this pathogen added to numerous processes contributing to Alzheimer's disease, including:

- Neuroinflammation,
- Neurodegeneration,
- Microgliosis and astrogliosis (an indication of brain injury),
- Formation of amyloid plaque, and
- Formation of neurofibrillary tangles.

Editor's Note: The researchers concluded that, "The neuropathological features observed in this study strongly suggest that low grade, chronic periodontal pathogen infection can result in the development of neuropathology that is consistent with that of [Alzheimer's disease]."

* *PLoS One*. 2018 Oct 3;13(10):e0204941.

Nicotinamide Shows Promise for Treating Fibrotic Eye Diseases

Nicotinamide, a form of vitamin B3, has been identified as a possible treatment for fibrotic eye diseases and could potentially prevent vision loss, according to a study published in *Stem Cell Reports*.*

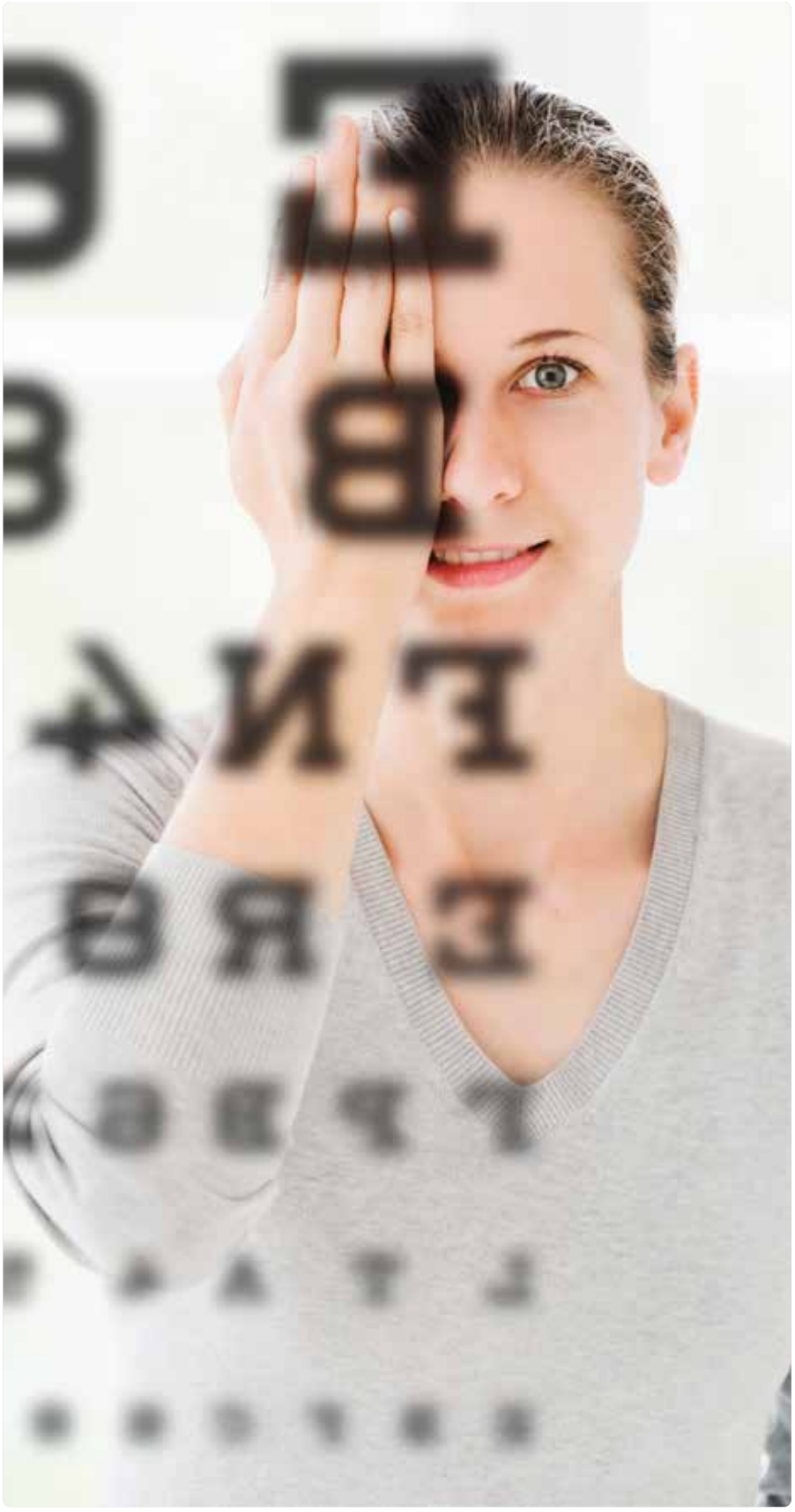
Fibrotic eye diseases occur when aggressive *cell transformations* during wound healing lead to scar tissue, retinal detachment, and ultimately, vision loss and blindness.

When researchers applied nicotinamide to human adult cells in vitro, they found that nicotinamide had three key mechanisms that make it a possible treatment for fibrotic eye diseases:

1. It **inhibits** harmful cell transformations.
2. It **reverses** the development of membranes associated with scar tissue.
3. It **slows** the development of eye diseases that can lead to vision loss and blindness.

Timothy Blenkinsop, Ph.D., the study's co-lead investigator, said, "This discovery helps evolve our understanding of wound healing, as well as good inflammation versus bad inflammation. Good inflammation essentially nudges the system into a regenerative response, while bad inflammation can create harmful scar tissue formation."

Editor's Note: "This is an exciting time to understand how this compound [nicotinamide] can be used to treat and reverse not only fibrotic diseases of the retina but other diseases too," Dr. Blenkinsop said.



* *Stem Cell Reports.* 2020 Apr 14;14(4):631-47.

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The Brain & Body Element

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

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Item #02403

1000 mcg • 100 vegetarian capsules

NON GMO LE CERTIFIED

This product is available at fine health food stores everywhere.

References

1. *Appl Physiol Nutr Metab.* 2018 Apr;43(4):412-4.
2. *J Clin Psychiatry.* 2015 Mar;76(3):319-26.
3. *Eur J Nutr.* 2011 Aug;50(5):387-9.
4. *J Alzheimers Dis.* 2015;48(2):403-10.
5. *JAMA Psychiatry.* 2017 Oct 1;74(10):1005-10.

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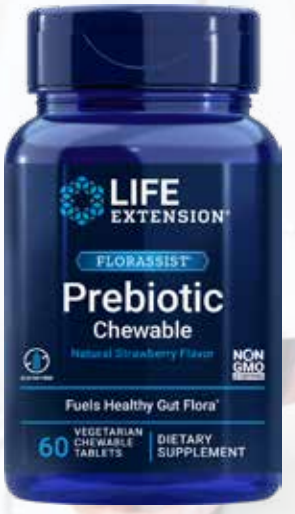

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- With age, our **bifidobacteria** levels decline to as little as **5%**, creating gut imbalance.[1]
- *Increasing* **bifidobacteria** levels *enhances* digestion and carbohydrate metabolism.
- *Strawberry flavored* **FLORASSIST® Prebiotic Chewable** helps restore healthy **bifidobacteria** levels in as little as 14 days using **XOS** prebiotic fiber.[2]
- **1,000 mg** of **XOS** (xylooligosaccharides) per prebiotic chewable.

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

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This product is available at fine health food stores everywhere.

Fracture Prevention

*About 1 in 2 women and 1 in 5 men will suffer an **osteoporotic fracture** after age 49.*[1]

WILLIAM FALOON

A report published in the ***Journal of the American Medical Association*** analyzed the degree of **osteoporotic fracture** reduction that occurred in response to **vitamin D** and **calcium** supplementation.[1]

This **meta-analysis** found that combining low doses of **vitamin D** (**400 IU** to **800 IU**) with high **calcium** intake (**1,000 mg** to **1,200 mg**) reduced risk of *any* **fracture** by **6%** and **hip fracture** by **16%**.

The problem is that more than **two million** fractures occur each year in the United States related to **osteoporosis**.[2]

If people rely *only* on **calcium** and **vitamin D**, this means **1.9 million** fractures will continue to occur each year.

To put today's **vitamin D** deficit in perspective, baseline vitamin D **blood levels** in the **vitamin D** *only* segment of this meta-analysis ranged from **10.6 ng/mL** to **26.3 ng/mL**.

This is far less than the **50 ng/mL** to **80 ng/mL** of ***25-hydroxyvitamin D*** blood levels that many groups consider optimal.

Observational studies included in this meta-analysis found that for each **10 ng/mL** increase in *25-hydroxyvitamin D* there was an associated **7%** reduced relative risk for *any* fracture and **20%** reduced relative risk for **hip fracture**.

The analysis published in the ***Journal of American Medical Association (JAMA)*** further validates how low-cost **nutrients** can decrease today's **osteoporosis/fracture** epidemic.

This editorial describes other methods to lower **fracture** risk.

Insufficient Potencies

The expectation that **calcium** and/or **vitamin D** can meaningfully protect against osteoporosis and fracture risk has caused a lot of studies to be designed in ways that often fail to show comprehensive bone benefits.

A meta-analysis published in ***JAMA*** showed a reduced **fracture risk** in response to vitamin D and calcium supplements. There was no benefit when taking **vitamin D** alone.[1]

A look at studies on vitamin D supplementation *alone* (included in this analysis) reveals baseline vitamin D **blood levels** ranging from **deficiency** at **10.6 ng/mL** to an **insufficient** level of **26.3 ng/mL** of *25-hydroxyvitamin D*.

The average **vitamin D3** dose used in these studies was **833 IU** a day.

Among the clinical trials in the vitamin D-*only* part of the meta-analysis, this low vitamin D dose (**833 IU**/day) was associated with a median blood level change of **8.4 ng/mL** of *25-hydroxyvitamin D*.

This means virtually none of the people evaluated in the ***JAMA*** study achieved **optimal** blood levels of *25-hydroxyvitamin D*.

Studies using low potencies have been the subject of misguided media reports claiming there is no value to taking **bone-building** supplements.

The reality is no single nutrient can be counted on to maintain **bone integrity** when confronted with the degenerative changes that occur with normal skeletal aging.

Vitamin Deficits Increase Fractures

A **2019** study linked **vitamin K** deficits and other deficiencies to increased **fracture** rates.[3]

In this study, a Japanese group looked at associations of **multiple** vitamin deficiencies and incident **fractures** in women.[3]

They used **homocysteine** blood levels as an indicator of **B-vitamin** status. Homocysteine is higher in people deficient in certain **B-vitamins**.

Blood levels of ***25-hydroxyvitamin D*** were used to assess **vitamin D** status.

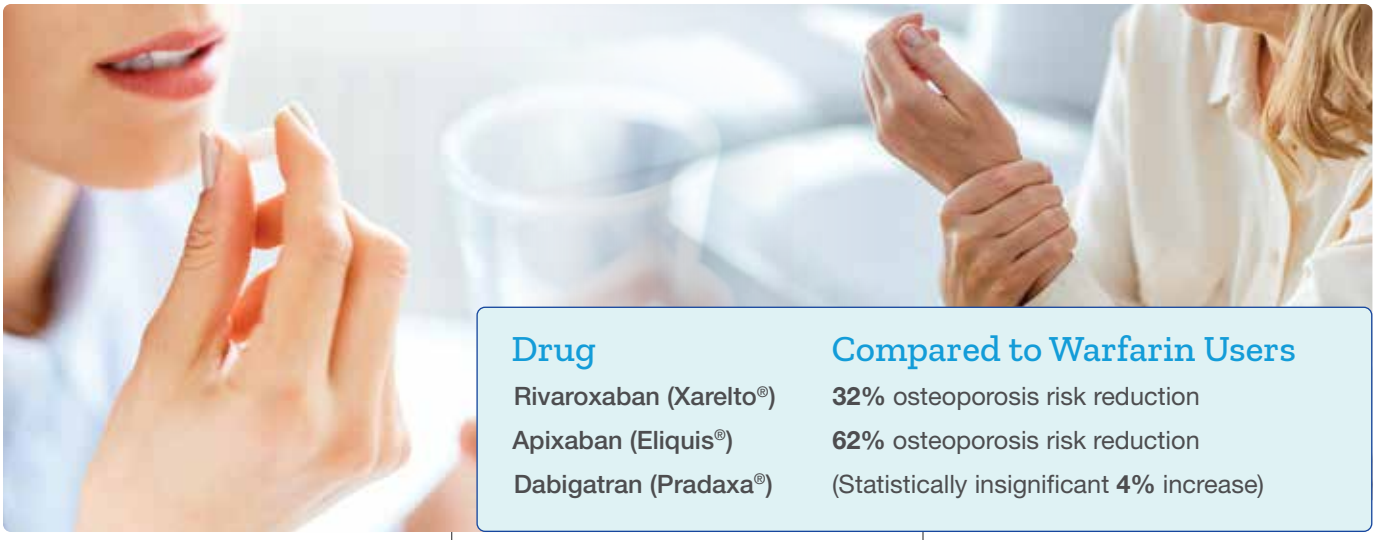
Vitamin K status was evaluated by measuring a protein (undercarboxylated **osteocalcin**) that vitamin K favorably influences to maintain **bone density**.

The **human** study subjects were divided into four groups:

- No vitamin deficiency
- Single deficiency (of either vitamin D, vitamin K or B-vitamins)
- Double deficiencies (of either vitamin D, vitamin K or B-vitamins)
- Triple deficiencies (of vitamin D, vitamin K and B-vitamins)

A total of 889 women were included in this analysis, with an average age of about **68** and average follow-up of about **6.3 years**.

Incident **fractures** were observed in **29.7%** of subjects This finding alone shows how frequent **fractures** are in women averaging only **68** years.



Drug	Compared to Warfarin Users
Rivaroxaban (Xarelto®)	**32%** osteoporosis risk reduction
Apixaban (Eliquis®)	**62%** osteoporosis risk reduction
Dabigatran (Pradaxa®)	(Statistically insignificant **4%** increase)

The study found that the *number* of **vitamin deficiencies** was associated with a **25%** increased risk of incident **fracture**. This association persisted even after adjustment for sources of potential confounding.

The authors of this study concluded:

"Accumulation of vitamin deficiencies was related to incident fractures."

This study supports data **Life Extension®** reported in the **1990s** showing the role of vitamin/mineral deficiencies in osteoporosis and **fracture risk**.[4]

Warfarin Users Beware

Those with atrial fibrillation, aortic valve replacement, deep vein thrombosis, and other conditions require powerful **anti-coagulant drugs** to reduce the risk of a clot forming inside a blood vessel (thrombosis).

For decades, the drug of choice in these situations was a **vitamin K antagonist** drug called **warfarin** (Coumadin®). Warfarin works by inhibiting the synthesis and activation of **vitamin K**.[5,6]

Not only does warfarin disable beneficial **vitamin K activity** (such as keeping calcium in bones and out of arteries), but warfarin users are put on strict diets that are extremely low in **vitamin K**.

As a result, long-term warfarin users may suffer **vascular calcification** and **bone loss,** as has been shown in some studies.[7,8]

Fractures in Warfarin Users

A study published in October **2019,** conducted in Denmark, looked at osteoporotic **fracture incidence** in people prescribed various types of **anti-coagulant** drugs. **Warfarin** was the only **vitamin K antagonist** drug while the other drugs did not have vitamin K antagonistic effects.[9]

This study found overall fracture risk was low in this population, but that those prescribed non-warfarin anticoagulant drugs (like Xarelto® and Eliquis®) had significantly lower risk of **osteoporotic fractures**.

A similar study published in January **2020** conducted in Taiwan looked at **atrial fibrillation** patients treated with warfarin or non-vitamin K antagonist drugs.[10]

Compared to warfarin treatment, drugs that did not block **vitamin K** were associated with an **18%** lower risk of osteoporosis.

The box at the top of this column shows the data obtained in the sub-group analysis of this study relating to different anti-coagulant drugs.

The study authors noted the lower **osteoporosis risk** became significantly better in those with *longer* treatment duration and concluded:

"Compared with warfarin, rivaroxaban and apixaban were associated with a significantly lower risk of osteoporosis in patients with atrial fibrillation."

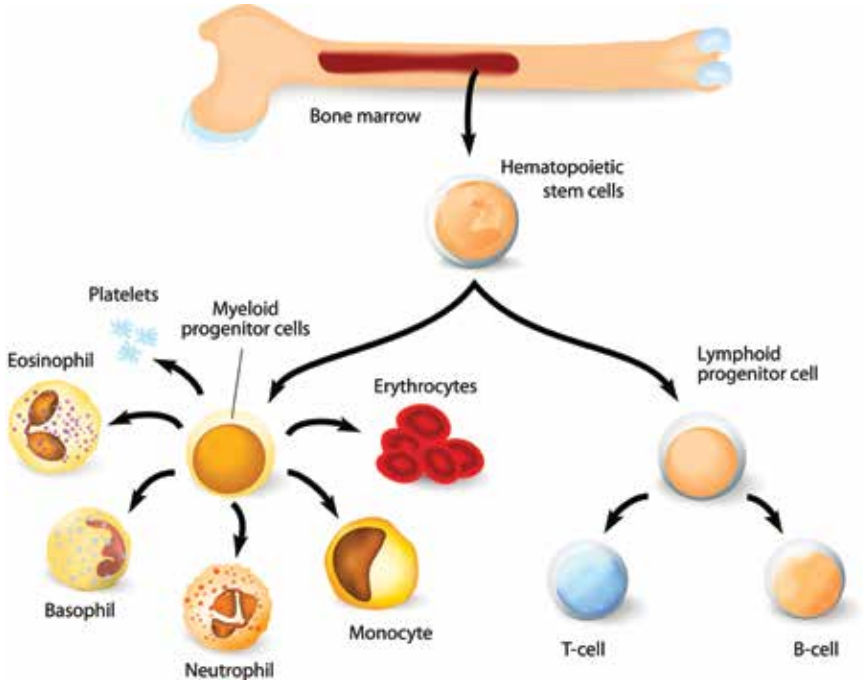
Life Extension® has suggested for decades that **warfarin** users consult their doctor about supplementing with a low dose of **vitamin K2** (**45 mcg** a day) and adjusting warfarin dose slightly upward to maintain desired **INR/pro-thrombin time** levels. This can enable one to achieve anti-coagulant benefits without completely depriving the body of vitamin K. More about vitamin K and warfarin can be reviewed at: www.LifeExtension.com/warfarin

Effect of Vitamin K on Bone Density and Fractures

As scientific debates continue, studies published in **2019-2020** point to a role that **vitamin K** has in maintaining healthy bones.

One meta-analysis of randomized, controlled trials found that the odds for a clinical **fracture** were lower in those supplementing with **vitamin K** compared to controls.[11]

Blood cell formation from differentiation of hematopoietic stem cells in red bone marrow.



Protecting Bone Marrow

The spongy tissue inside our **bones** is known as the **bone marrow**. It contains **stem cells** that can develop into immune cells, red blood cells, mesenchymal stem cells, and platelets.

Given the involvement of bone-marrow-derived cells in the maintenance and formation of the different blood cellular components, a group of researchers investigated how the vitamin K antagonist drug **warfarin** can adversely impact the **bone marrow** microenvironment including mesenchymal stem cells, macrophage immune cells and vital **hematopoietic stem cells**.[13]

Using various in vitro assays, this group showed how **vitamin K antagonists** adversely alter bone physiology and cause a staggering **eight-fold** reduction in functional **hematopoietic stem cells**.

These scientists pointed out that **vitamin K antagonist** drugs (like warfarin) are not directly toxic to **hematopoietic stem cells** but impair them via other mechanisms.

Without providing a causal link, this paper associates the use of vitamin K antagonists with a potential increased risk of **myelodysplastic syndrome.**

About three out of every 10 patients with **myelodysplastic syndrome** (about **30%**) develop **leukemia,**[14] which is notoriously difficult to treat.

More human research is needed to assess the ability of **vitamin K** in maintaining healthy **bone marrow.**

The authors of this same study, however, said there was "***insufficient***" evidence to confirm these findings in post-menopausal or osteoporotic patients and that:

"There are too few trials to draw conclusions for other patient groups."

My rebuttal to these pessimistic conclusions is that many vitamin K trials use lower-than-optimal doses of vitamin K and some use only vitamin **K1**, which does not convert into **vitamin K2** in all persons.[12]

And of course, I would never say **vitamin K2** by itself is enough to provide comprehensive **skeletal support**, as evidenced by the Japanese study cited earlier whereby multiple **nutrient deficiencies** markedly increase **fracture** incidence.

Review of Accumulated Evidence

A review of the accumulated evidence that vitamin K plays a protective role in **age-related** disorders such as cardiovascular disease, osteoarthritis and osteoporosis was published in August **2019**.[15]

This assessment identified novel roles that have emerged for vitamin K that extend *beyond* its ability to keep **calcium** in **bones** and out of one's **arteries** and soft tissues.

Of interest was evidence that vitamin K reduces "**inflammaging**" by suppressing **NF-kB** (nuclear factor-kappa B).[15]

This **2019** review highlights the valuable **whole-body** benefits that can be attained with proper **vitamin K** status.

Bones Need Hormones

The major regulator of **bone remodeling** in men and women is the sex hormone **estrogen**.[16]

Other hormones that influence bone density include **testosterone**, **DHEA**, and **growth hormone**.[17,18]

With aging, many of these hormone levels plummet and accelerate loss of **bone density**.

Many men and women use bioidentical hormone replacement therapy to maintain youthful hormone levels and support healthy bones.

Comprehensive **blood tests** enable maturing men and women to achieve optimal **hormone balance**.

Pregnenolone is a "mother" hormone that can cascade in the body into bone-supporting hormones estrogen, progesterone, testosterone, and DHEA.

A review article published in **2020** describes many of the **anti-aging** properties of **DHEA** including its potential to help maintain strong **bones**.[17]

Restore Bone Integrity

No single therapy adequately protects against **skeletal deterioration** that occurs with normal aging.

A comprehensive set of **interventions** should be considered, including cutting back on unhealthy lifestyle choices and ensuring that adequate potencies of *every* bone-building nutrient and hormone are consumed.

Some individuals may wish to consider bioidentical hormone replacement to ensure optimal hormone balance.

I know that many of you are engaging in **intermittent fasting** or other forms of reduced calorie intake.

While there are enormous benefits to these practices, a potential downside is that one may not ingest enough calcium, magnesium, boron, vitamins D and K, and other nutrients required to maintain **bone density**.

The good news for consumers is that bone-building, multi-nutrient formulas are affordable because the ingredients they contain (calcium + magnesium + boron + vitamins D + K) are not expensive.

You can further enhance **bone health** by avoiding lifestyle factors that increase **fracture risk** and discuss with your doctor whether any of your medications (such as warfarin or proton pump inhibitors) might be undermining your bone strength.

What Causes Bone Loss?

Bone is living tissue that undergoes a continual self-regeneration process called **remodeling**. Remodeling removes old bone and replaces it with new bone.[19,20]

With **aging** this balance shifts to favor greater bone **removal** (resorption) and less new bone **formation**.

The result is **osteoporosis** and increased **fracture** risk.[21]

A variety of factors markedly accelerate loss of bone density and strength. Of course menopause is one, but also the use of drugs like **corticosteroids** and **proton-pump inhibitors** (PPIs), smoking tobacco, drinking excess alcohol, and anti-testosterone treatment for prostate cancer (known as hormone ablation) are a few of the most notable culprits.[22-25]

Weight-bearing exercise, good nutrition, and maintaining hormone balance help protect aging bones.[26,27]

Health-conscious individuals are often surprised when a **bone density** test reveals **osteopenia** (loss of bone density, but not to a degree that increases fracture risk) or **osteoporosis** (deterioration in bone density with increased fracture risk).[28]

Maturing people should recognize that **bone density** peaks early in life (between 18-30 years) and progressively declines thereafter.[29]

In This Month's Issue…

Calorie restriction can extend healthy longevity, but few people consistently adhere to reduced food intake. Certain **nutrients** are discussed on page 36 that mimic biological effects that occur in response to reduced food intake.

A hallmark of cellular aging is damaged **DNA**. An article on page 58 describes the ability of **tocotrienols** to protect against DNA damage that accelerates systemic aging.

If you wonder where all this is leading, page 48 has an exclusive interview with Harvard geneticist **Dr. George Church** who is developing **gene therapies** aimed at eliminating all human **viruses** and reversing biological **aging**.

The steps taken to protect against **degenerative aging** today will enable more of you to benefit from extended healthy lifespans that may be less than 10 years away.

For longer life,

William Faloon, Co-Founder to Life Extension Foundation Buyers Club, Inc.

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Laboratory studies show evidence of **systemic rejuvenation** when the **senescent cell** burden is reduced.*

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**Aging Cell.* 2015 Aug;14(4):644-58.

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Nutrients to *Charge Up* BRAIN FUNCTION

BY JASON MCNEIL

Nootropics are compounds that *enhance* **cognition** and facilitate **learning**.

They differ from nutrients that protect against **brain aging**.

Nootropics are for people seeking to *improve* brain **processing speed** and **mental alertness**.

Nutrients with **nootropic** properties have become popular for people of all ages to improve thinking speed and accuracy.

Nootropics Tune Up Your Mind

Nootropics are a different type of brain and cognition supplement. Their goal is to boost cognitive performance *now*.

Nootropics are meant to improve and recall recent and old memories.

Nootropic compounds boost cognitive efficiencies by helping brain cells operate at **peak power**.

Scientists have identified nutrients shown in clinical (human) studies to improve cognitive function, processing speed, and memory.

Bacopa Monnieri Improves Learning

As we age, our ability to process and absorb new information begins to decline.

In seeking to create a plant-based nootropic, researchers focused on compounds associated with **cognitive enhancement** in **human** studies. One key aspect of improved cognition is improving the brain's ability to ***learn*** and ***retain*** information.

Research on the flowering herb ***Bacopa monnieri*** reveals improved memory. In ancient times, the herb was given to scholars to improve their learning and memorization of vast religious texts that were orally handed down from generation to generation.[1]

In several **clinical trials,** *standardized* extracts of *Bacopa* have been shown to sharpen several aspects of cognitive function, specifically learning rate and retention of information.[2-9]

These human studies also show that *Bacopa* improved additional aspects of cognitive functions such as:

- Auditory verbal learning speed,
- Speed of visual processing,
- Working memory,
- Formation of new memories,
- Recall of memories, and
- Power and speed of attention.

In animal studies, *standardized* extract of *Bacopa* also improved brain activity by promoting the growth of neuron connections in the **hippocampus** and amygdala, another part of the brain involved in perception of emotions.[10-12] The hippocampus is one of the most important brain regions for the formation of new memories. Other benefits included:[1,12,13]

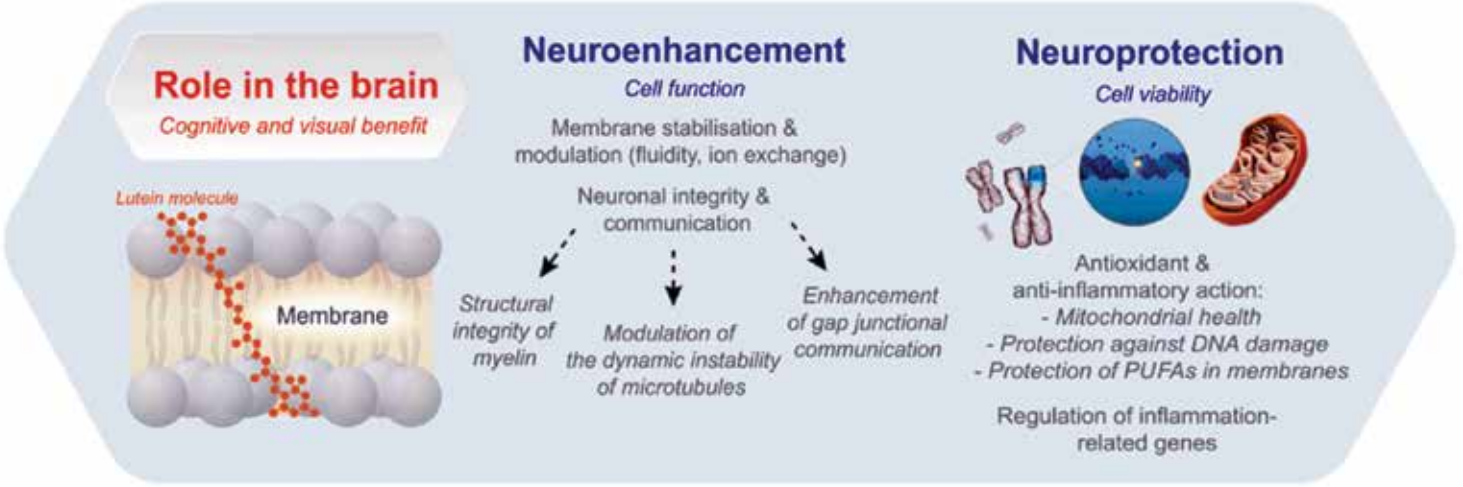
- Improved spatial learning,
- Increased dendritic length and branching,
- Modulation of neurotransmitter production,
- Increased synaptic concentration,
- Reduced brain inflammation,
- Increased cerebral blood flow, which reduces oxygen and nutrient deficits, and
- Increased nourishment of neurons.

Gotu Kola Improves Reaction Time and Accuracy

The next step in creating a multi-function nootropic was investigating the herb **gotu kola**.

Gotu kola is a flowering herb native to Asia. It has also been used to boost brain power in traditional Eastern medicine for centuries.

Lutein + Zeaxanthin Supports Neuronal Communication



Lutein and zeaxanthin: The possible contribution, mechanisms of action and implications of modern dietary intake for cognitive development in children. ***HRB Open Res.*** **2019;2:8.**

In one clinical trial of healthy, older adults, daily intake of standardized extract of **gotu kola** for two months led to significant improvements in several aspects of brain function.[14]

Using **electroencephalography** (EEG), the electrical activity of the brain was recorded and combined with cognitive testing. Researchers saw evidence of improved **attention** and **reaction time** in mental tasks just one hour after supplementation. These improvements in reaction time indicate improved brain processing speed.

By the end of the two-month study, other improvements in cognitive function were seen, including short-term **working memory**, **word recognition**, **spatial memory** and **picture recognition**, and **alertness**.

Gotu kola also improved **mood** and **calmness**. This has implications for managing anxiety and depression, which can interfere with peak mental clarity.[15]

In another study, patients with generalized anxiety disorder who supplemented with **gotu kola** noted significantly improved levels of anxiety and stress.[16]

Gotu kola has also demonstrated benefits in animal studies.[17,18] In a mouse model of **dementia**, animals given extracts of **gotu kola** performed significantly better than untreated animals in tests of **learning** and **memory**.[18]

WHAT YOU NEED TO KNOW

A Powerful Nootropic Formula

- **Nootropics** are compounds and nutrients meant to enhance cognitive abilities in healthy individuals.
- **Life Extension®** scientists have identified four such plant nutrients, which have *individually* demonstrated the ability to ***improve brain function***.
- The carotenoids **lutein** and **zeaxanthin** and standardized extracts of the flowering herbs **gotu kola** and ***Bacopa monnieri*** have each been shown in clinical trials to enhance cognitive abilities, improve memory and learning, brain processing speed, and more.

The Eye-Brain Connection

Carotenoids are a group of pigments found in many fruits and vegetables.

Two closely related carotenoids, **lutein** and **zeaxanthin**, are taken up and concentrated in the **retina** of the eye, the tissue that senses light and sends information to the brain for visual recognition via the optic nerve.

Lutein and zeaxanthin have long been shown to protect **macular density** necessary for **visual function**.[19-24] These carotenoid pigments help maintain sharp sight while protecting the retina from damage due to blue light, chronic inflammation, and other threats.

Scientists have discovered that significant amounts of **lutein** and **zeaxanthin** also concentrate in the **brain**.

This isn't very surprising, since the **retina** is technically an **extension of the brain** that contains **nerve cells** similar to those found in the brain itself.[25-29]

Levels of **lutein** and **zeaxanthin** in the eye and the brain are directly correlated.[25-29] That means testing their levels in the eye, which is easier to do, allows scientists to also estimate the levels of lutein and zeaxanthin in the brain.

People with the *highest* plasma and macular levels of **lutein** and **zeaxanthin** also have the *highest* **cognitive function**.[27,30-35]

Using advanced MRI imaging technology, researchers were able to show that *higher* levels of **carotenoids** in the **brain** were associated with better **efficiency of the brain cells** during tests of learning, memory, perception, decision-making, and motor coordination.[33]

Human Studies of Lutein and Zeaxanthin

Based on findings that **lutein** and **zeaxanthin** function as nootropics, researchers identified a source derived from marigold flowers.

The combination of **lutein** and **zeaxanthin** has been tested in **nine** human studies on brain function in a wide age range.[36-44]

Scientists found that oral intake of lutein-zeaxanthin leads to improvements in brain speed, efficiency, and overall cognitive function.

Research shows that lutein and zeaxanthin improved **brain function** through:[43,45]

- Improved neuronal communication,
- Increased neural integrity,
- Enhanced memory retention, and
- Increased processing of visual signals.

In healthy young adults, **10 mg of lutein** and **2 mg of zeaxanthin** daily resulted in *significant improvements* in **memory**, **reasoning**, and **complex attention**—the ability to hold complicated ideas in the mind, assess them, and quickly act on them.[41]

This improvement in complex attention indicates that brain processing speeds were increased, allowing individuals to better assess complex stimuli and react appropriately.

Similar findings have been seen in older adults. The same dosage of lutein and zeaxanthin improved complex attention and other aspects of cognition in subjects averaging **73.7 years** of age.[40]

In another study of older adults, oral lutein and zeaxanthin helped maintain learning and memory while improving brain blood flow, while these functions deteriorated in participants who received a placebo.[39]

Scientists believe lutein and zeaxanthin work, in part, by wedging themselves into the walls of brain **cell membranes**.[25,45-48] This may boost the membrane's functional properties and improve other aspects of membrane integrity.

Summary

The field of **nootropics** research aims to find compounds and nutrients that can boost cognitive performance.

A combination of nootropic compounds has been formulated to enhance **brain function**.

The carotenoids **lutein** and **zeaxanthin**, which are concentrated in the eye and brain, can improve and protect visual *and* mental function.

Standardized extracts of **gotu kola** and ***Bacopa monnieri*** each enhanced several aspects of cognitive function and mood in clinical trials.

This combination may help people of all ages achieve their full neurological potential.

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

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SUPPORT YOUR AGING IMMUNE SYSTEM

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Cistanche

- Supports longer lifespan in animals.[1]
- Optimizes ratios for key cells that indicate a more youthful immune system.[1]

Pu-erh Tea

- Boosts natural killer and naïve T cells while decreasing interleukin-6 (IL-6).[2]

Reishi

- Helps inhibit biomarkers of immune senescence.[3]

Item #02005

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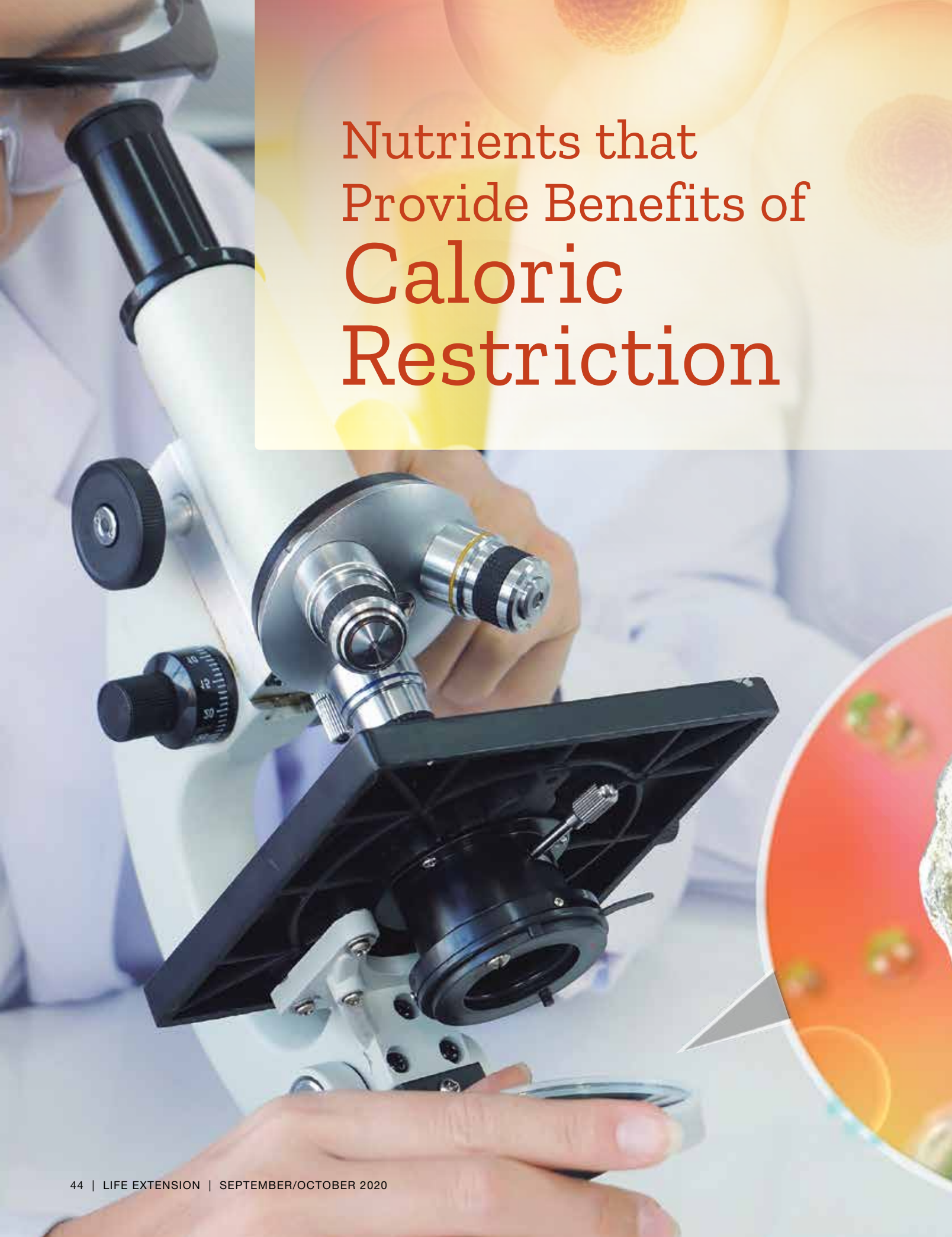
Nutrients that Provide Benefits of Caloric Restriction



BY NANCY KOVACS

Published studies on a wide range of organisms show:

Caloric restriction can improve health and ***extend life***.[1-3]

But people are challenged when trying to chronically reduce their food intake.[1]

Even those who initially succeed often return to regular eating, losing out on the **longevity** benefits that caloric restriction can offer.

Researchers have identified **plant-derived** compounds that help **activate** similar health-promoting cellular responses as **caloric restriction**.

How Caloric Restriction Prolongs Life

Caloric restriction means **limiting** the number of calories consumed each day, while avoiding malnutrition.

Restricting calories extends life and reduces age-related chronic disease in many organisms.[2,3] These effects have been observed in a wide range of animal models, including mammals.

When caloric intake is *low*, during what's known as a **fasting state**, cells switch into protective mode. They activate processes that rejuvenate themselves and defend against potential threats and stressors.

These changes have long-term benefits for overall health, and possibly for life extension as well.

On the flip side is the dietary excess plaguing modern societies. This chronic, surplus calorie ingestion contributes to a variety of health problems.

Surging rates of obesity, type II diabetes, neurodegenerative disorders, and cancer have all been linked to excessive calorie intake.

Scientists have pinpointed some of the specific cellular changes that occur with caloric restriction. The most practical ways of achieving these benefits are:[4-10]

1. Boosting function of **sirtuins**, proteins that regulate cellular health,
2. Increasing activity of **AMPK**, an *enzyme* that regulates metabolism,
3. Reducing activity of **mTOR**, a protein linked to aging and chronic disease,
4. Blocking **cellular senescence**, when older cells become dysfunctional, and
5. Encouraging **autophagy**, cellular "housekeeping."

These actions protect against many forms of chronic disease and accelerated aging.[4,6-10]

GYNOSTEMMA PENTAPHYLLUM

Caloric Restriction and Intermittent Fasting "Mimetics"

Sticking to a restrictive diet is difficult.

It can also be unpleasant. For some, substantial caloric restriction may lead to loss of strength and stamina, loss of libido, loss of bone density, depression, and other undesirable effects.[1]

Research is increasingly finding that there are alternatives to severe dietary restriction. Several compounds have been shown to target some of the same cellular **pathways** as caloric restriction, without side effects.[5,7-9,11]

These compounds are known as caloric restriction **mimetics**. A mimetic is something that mimics the effects of something else.

Some of the nutrients found to be caloric restriction mimetics are health-promoting **polyphenols**.

For each of the five major cellular changes spurred by caloric restriction, science has discovered mimetics that have the same effects.

1. Boosting Sirtuin Function

One way caloric restriction extends lifespan is by ramping up the activity of signaling proteins called **sirtuins**, particularly **SIRT1**.[6-8]

Sirtuins regulate cellular health and defend cellular components in times of stress. They shield **DNA** from damage that speeds the aging process and makes cells susceptible to disease.[12,13]

Studies show that improving **sirtuin function** extends lifespan of various organisms.[12,14-18]

The polyphenol **resveratrol**, found in minute quantities in red wine, grapes, and berries, activates **SIRT1**.[14-16,19,20]

In mice, resveratrol helps *mimic* the changes induced by dietary restriction, reducing the signs of aging.[11]

Resveratrol has been shown to stabilize DNA and extend lifespan of yeast by a whopping **70%**.[19]

While resveratrol *activates* sirtuins, a cofactor called **NAD+** (nicotinamide adenine dinucleotide) is required for **sirtuins** to *function* properly. With advancing age, **NAD+** levels drop.[12,13]

The oral **NAD+** precursor nicotinamide riboside boosts NAD+ cellular levels rapidly, helping to support healthy **sirtuin** function.[21-23]

Taken together, resveratrol and nicotinamide riboside maximize the benefits for cellular health and longevity.

2. Activating AMPK

Another longevity-promoting change spurred by caloric restriction is increased **activity** of an *enzyme* called **AMPK**.

Stimulating AMPK has a critical impact on metabolism. It helps prevent weight gain, improves insulin sensitivity, and reduces high blood glucose levels.[24-27]

The most commonly prescribed medication for type II diabetes is **metformin**, which works partially by activating AMPK.

A number of **plant-derived** compounds are also potent activators of AMPK.

Gynostemma pentaphyllum is known as the "immortality herb" in some Asian cultures. Cell and animal studies have shown that *Gynostemma* extracts activate **AMPK**, resulting in health benefits that include reduced body weight and improved cholesterol levels.[28-32]

In a **2019** study of mice fed an obesity-inducing diet, *Gynostemma* prevented weight gain, reduced fat mass, and improved blood lipid markers.[33]

AMPK also stimulates **SIRT1**. In this 2019 study, animals receiving ***Gynostemma*** had an approximately **4.5-fold** increase in SIRT1 expression compared to untreated animals.

Hesperidin is a plant compound found in citrus fruits that has also been shown to amplify AMPK activity.[34-37] In mice, it lowers body weight and lipid levels while improving insulin sensitivity and glucose control.[35]

In humans, **500 mg** of hesperidin daily was found to lead to improvements including better blood vessel reactivity and reduced body-wide inflammation.[36]

WHAT YOU NEED TO KNOW

The Benefits of Caloric Restriction Without Fasting

- **Caloric restriction** has powerful anti-aging effects, reducing chronic disease and extending life, as shown in many studies.
- Restrictive diets are difficult to adhere to and have potential unpleasant side effects.
- Scientists have identified crucial cell changes that are induced by dietary restriction. These include **sirtuin** activation, boosting **AMPK**, reducing **mTOR** activity, protecting against cell **senescence**, and promoting beneficial **autophagy**.
- Several plant-derived nutrients *mimic* the cellular effects of restricting calories, producing some of the same protective benefits.
- **Resveratrol**, **nicotinamide riboside**, ***Gynostemma pentaphyllum***, **hesperidin**, **curcumin**, **quercetin**, **theaflavins**, and **apigenin** are nutrients that closely imitate the beneficial effects of restrictive diets.

3. Decreasing mTOR Activity

mTOR stands for the "**mechanistic target of rapamycin**."

In youth, balanced **mTOR** activity enables rapid growth.

If **mTOR** activity remains stuck in high gear as people age, it contributes to a number of deleterious effects.

When nutrients are plentiful, **mTOR** activity goes up.

If **mTOR** is not balanced, aging individuals could accumulate unwanted fat stores even when they don't ingest calories excessively.

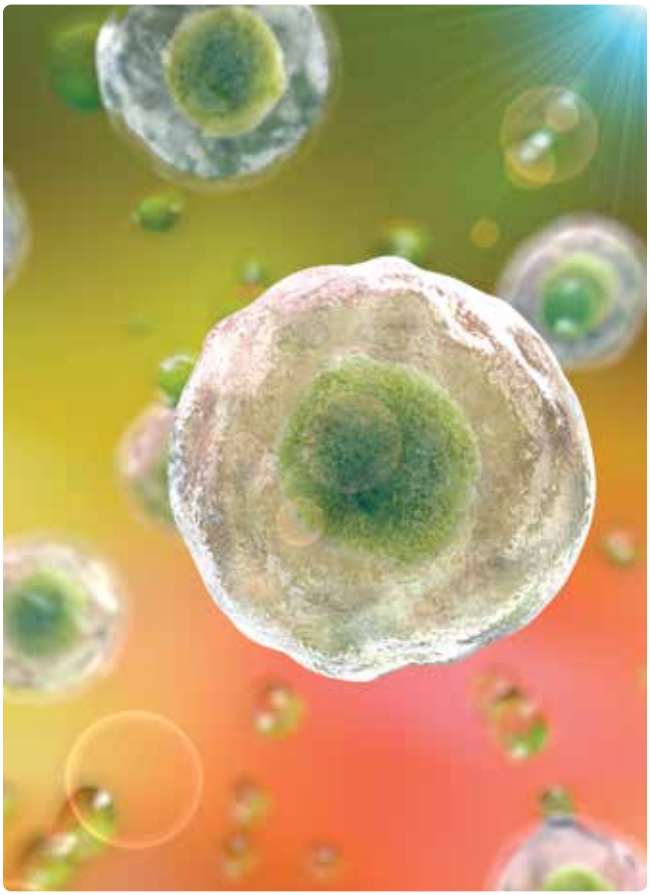
Caloric restriction *decreases* mTOR activity, protecting health.[8]

Research shows that **resveratrol** and **curcumin**, a compound found in **turmeric** root, have mTOR-inhibiting activity.[38-42]

4. Preventing Cellular Senescence

As cells age, many become dysfunctional and lose the ability to grow or divide. This is referred to as **cellular senescence**.

Senescent cells secrete compounds that damage surrounding cells and promote **chronic inflammation**.



Cellular senescence is a major driver of aging of tissues, loss of function, and development of disease.

Caloric restriction limits the development of senescent cells, shielding tissues from their harmful effects.[6]

Compounds called **senolytics** can help reduce the senescent cells' burdens without caloric restriction.

The most studied senolytic therapy combines the plant pigment **quercetin**, found in many fruits and vegetables, with the chemotherapy drug **dasatinib**.

Several studies show this two-compound cocktail (dasatinib + quercetin) decreases the number of **senescent cells** in tissues, reducing signs of aging and diminishing the occurrence and severity of chronic disease.[48-51]

Early human trials of this therapy are showing promising results, but dasatinib is a synthetic pharmaceutical drug.[48,52] As a result, many people today would prefer a safer **senolytic** compound.

Scientists have found another way to remove senescent cells, using **plant-based** nutrients found in commonly consumed food and beverages.

Quercetin on its own possesses senolytic properties,[53] and **theaflavins** from black tea act in similar cell signalling ways as dasatinib.[54-56]

Recently, researchers have made another advance in **senolytic** therapy. They've found that **apigenin** (a plant compound) reduces harmful compounds that **senescent cells** emit.[57,58]

By combining a *highly absorbable* **quercetin** with **theaflavins** and **apigenin,** scientists have created a plant-based formula, available without a prescription, that provides senolytic action without resorting to pharmaceutical drugs.

And even more exciting is the advent of **bioavailable fisetin** that may be the most effective way to remove senescent cells from aging bodies. Look forward to a novel and low-cost **bioavailable fisetin** in the near future.

5. Enhancing Autophagy

As cells get older, they accumulate damaged and worn-out components that interfere with the proper functioning of the cell.

In earlier stages of their life, cells do a kind of "housekeeping" on a regular basis. This involves removing older, damaged components inside cells and replacing them with new, healthy components. This process is referred to as **autophagy**.

With advancing age and poor diet, **autophagy** declines and cell clutter builds up, robbing tissues of their healthy cellular function. Deficient autophagy contributes to many diseases of older age.[59]

Caloric restriction has been shown to stimulate autophagy, refreshing and rejuvenating cells.[4]

A number of nutrients found in plants, particularly **resveratrol** and **curcumin**, have also been shown to stimulate healthy **autophagy**.[59-63]

Studies indicate this has protective effects against cancer, neurodegenerative disorders like Alzheimer's disease, and other chronic diseases.[59-63]

Look forward to specific plant-derived **autophagy-inducers** being introduced in **2021**. In the meantime, it's good to know that nutrients most readers of this magazine already supplement with have internal **cell-cleansing** properties.

Summary

Caloric restriction is one of the most widely studied methods to prevent disease and extend lifespan.

For people, adhering to rigorous dietary regimens can be difficult, if not impossible.

Scientists have identified cellular processes that are favorably altered by calorie-restricting diets.

Several plant-derived nutrients have been shown to mimic many of the effects of dietary restriction.

Resveratrol and **nicotinamide riboside** boost and maintain healthy levels of protective **sirtuin** function.

Gynostemma pentaphyllum and hesperidin activate the metabolism-regulating enzyme **AMPK**.

Resveratrol and **curcumin** limit harmful activity of the protein mTOR, while stimulating autophagy, or cellular "housekeeping."

Theaflavins and highly absorbable **quercetin** reduce the numbers of old, dysfunctional senescent cells in tissues. And **apigenin** reduces harmful compounds that **senescent cells** emit.

These effects help mimic the longevity-promoting impact of **caloric restriction**. •

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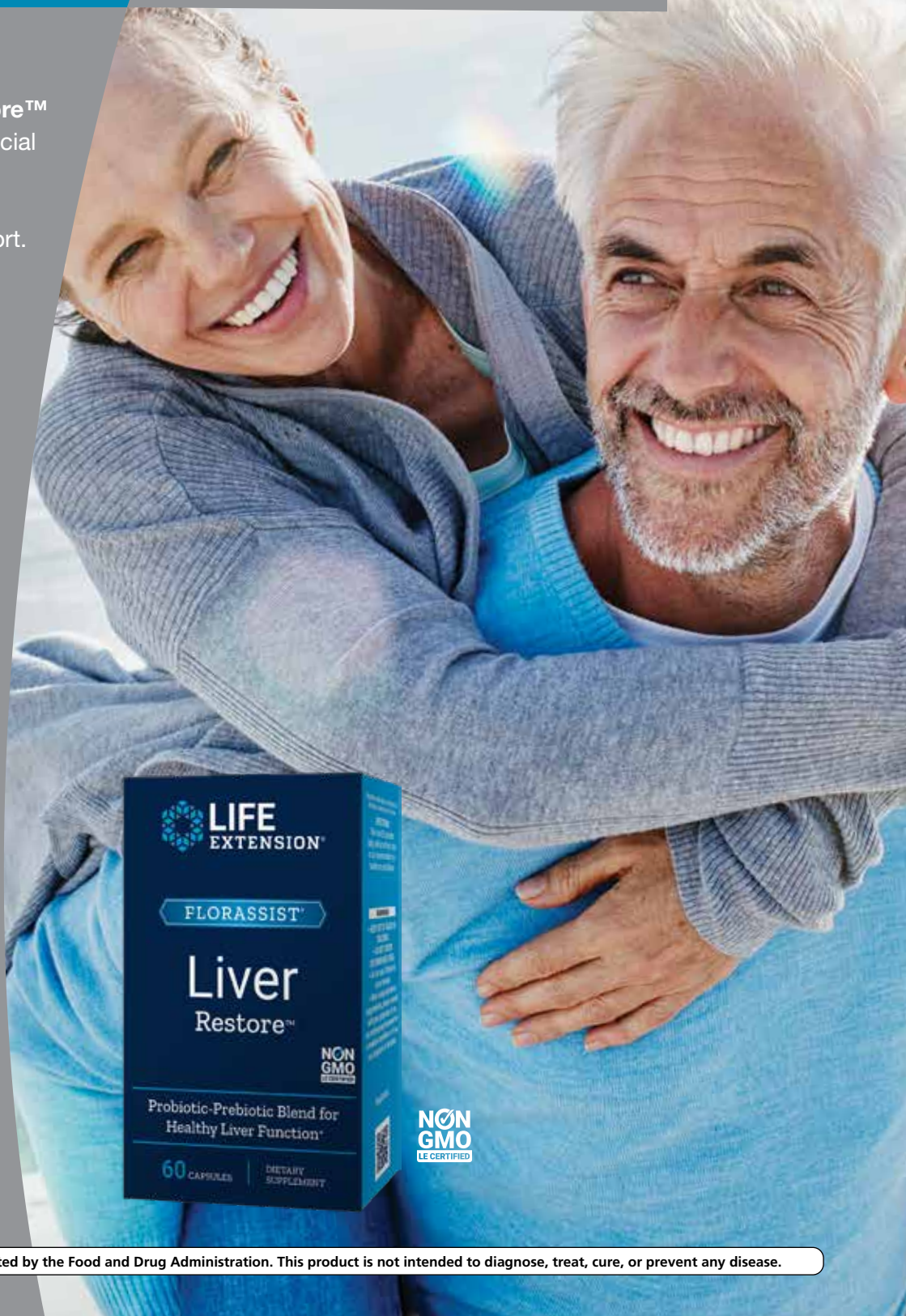

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WHEY'S
Longevity Benefits

BY MICHAEL DOWNEY

For years, **whey protein** has been taken by athletes seeking to increase muscle mass and performance.

Evolving research shows that **whey** does much more.

Whey helps protect against **muscle-wasting** and **weight gain**, while lowering certain **cardiovascular risk** factors.[1-11]

Glutathione levels drop with age, and this could play a role in **neurodegeneration**, reduced **immunity**, and other **age-related** conditions.[16-20]

Whey protein enhances **glutathione** production.[12,13]

The ability of whey to increase **glutathione** levels comes from its unique combinations of small **peptides**.

Whey protein is increasingly seen as a superfood for healthy longevity.

Dangers of Low Protein

About **45%** of older people in the U.S., and more than **84%** in residential care facilities, are *not* adequately nourished.[21,22] This results from reduced appetite and food intake, impaired nutrient absorption, and other age-related changes.[22-24]

Insufficient intake of quality protein can lead to **loss of muscle mass**,[25] especially in older individuals. After age 70, muscle mass decreases by about **15%** per decade.

However, this process begins as early as age 40, with an estimated **8%** loss of muscle mass per decade.[24]

Approximately **5%-13%** of people aged 60 or over experience age-related muscle-wasting so severe, it increases the risk of falls and disability.[26-28]

Inadequate protein consumption is associated with increased risk of age-related conditions like loss of bone strength and poor immunity.[29]

In fact, low protein intake is associated with **frailty**,[30] when the body is so weak it becomes unable to cope with stress or injury. Frailty is a strong predictor of mortality in aging people.[21,31]

Whey is a potential solution.

Whey Inhibits Muscle-Wasting

Made from the liquid part of milk that separates during cheese production, whey is a **high-quality protein source** for aging people.

It is also a great source of **branched-chain amino acids**, essential nutrients that reduce muscle breakdown and stimulate the creation of *new* protein in muscle.[32]

The most metabolically active branched-chain amino acid in whey is **leucine**. It activates signals in muscle that boost the body's anabolic (growth-promoting) drive, spurring muscle synthesis. [2,33-36]

In one study, hospitalized, frail, elderly men and women were given whey daily during their hospital stay. Compared to patients who didn't take whey, those who did had significant improvements in grip strength and knee extensor force, and improved rehabilitation outcomes.[6]

Boosting Muscle Mass

Whey doesn't just help *prevent* muscle loss. Two studies show that it also significantly ***increases*** **lean muscle mass**, perhaps especially when combined with exercise.

In a randomized, controlled trial, researchers divided 81 healthy, older women, aged 65-80, into three groups. Over 24 weeks, one group exercised twice weekly, another took **whey protein** but didn't exercise, and the third took the same amount of whey protein *after* exercising.[4]

The increase in muscle mass was significantly *higher* for the **whey + exercise group** than the other two groups. There was also a significant increase in grip strength and gait speed.[4]

Researchers also conducted a study to assess whey's effects on muscle loss following periods of *inactivity*.

In a controlled trial, men and women in their late 60s consumed a diet in which **45%** of their protein came from either whey or animal peptides. After two weeks of habitual activity, participants spent two weeks being **inactive**, then returned to normal activity for one more week (recovery).[1]

During the inactive periods, lean leg mass was reduced in both groups. During the recovery week, lean leg mass increased ***only in the whey protein group***.[1]

Preventing Weight Gain

Our metabolism naturally slows as we age, causing many to **gain weight**.

Whey has been shown to help **prevent weight gain**. Scientists have even considered it as a potential application for the **treatment of obesity**.[37]

In a host of studies, researchers discovered that the proteins, amino acids, and minerals in whey boost **satiety** (the feeling of fullness), benefit **glucose homeostasis** (the regulation of blood sugar levels), and optimize lean body mass.[38-42]

Scientists conducted one recent study on 100 men aged 70 or older with **sarcopenic obesity**, characterized by low lean mass and high fat mass.[10]

WHAT YOU NEED TO KNOW

The Benefits of Whey

- **Whey protein** has long helped athletes build muscle mass, but it does much more.
- Staying active and healthy with aging requires strong, healthy muscles. Unfortunately, aging adults are increasingly susceptible to losing muscle mass as they grow older.
- Whey is documented to help prevent the loss of muscle mass, inhibit weight gain, and reduce multiple risk factors for cardiovascular disease.
- Whey protein helps enhance the muscle-building effects of exercise while boosting glutathione levels.

They divided the subjects into three groups. One received no treatment, another received **whey protein** *only*, and the third received **whey protein** and underwent whole-body **electrical muscle stimulation** (which "exercises" the muscles). In addition, all subjects received **800 IU/day** of vitamin D.[10]

Total body fat, trunk body fat, and waist circumference were significantly reduced in *both* intervention groups (**whey protein** alone or combined with **electrical muscle stimulation**) after 16 weeks, but not in the untreated group.[10]

Another analysis of randomized, controlled trials on overweight and obese people concluded that there was a significant decrease in **body weight** *and* total **fat mass** in those who took **whey protein**.[11]

Fighting Cardiovascular Disease

Cardiovascular disease is the leading cause of death in the U.S.

Hypertension is one of the main factors contributing to cardiovascular disease.[43] Research shows that whey-based peptides may help reduce this risk factor.[44,45] (Peptides are chains of amino acids that are smaller than proteins.) And food-derived peptides like the kind found in whey are far safer than anti-hypertension drugs.

In a study, researchers asked 27 adults with mild **hypertension** (high blood pressure) to eat a high-fat breakfast and lunch along with **28 grams** of whey protein. This was later repeated with **28 grams** of **calcium caseinate**, a protein derived from casein (non-whey protein) in milk, and **27 grams** of the carbohydrate **maltodextrin**.[5]

Whey was found to reduce **systolic blood pressure** (the pressure on vessels when the heart contracts), by an average of **15.2 mmHg** compared to calcium caseinate, and **23.4 mmHg** compared to maltodextrin, for up to five hours after ingestion.

Whey also **reduced arterial stiffness** compared to maltodextrin. All these actions show whey's potential to improve cardiovascular risk factors.[5]

Scientists examining previous trials on **overweight and obese** patients also found that whey protein reduced body weight and significantly lowered blood pressure, glucose levels, and cholesterol, reducing the risk of cardiovascular disease.[11]

Summary

Whey protein is often viewed as just a protein source for bodybuilders.

Whey has also been shown to stop muscle-wasting in the elderly, boost lean muscle mass, prevent weight gain, and lower risks of cardiovascular disease and other illnesses.

It's increasingly recognized as a food to protect against degenerative aging and prevent muscle loss.

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What Type of Whey is Right for You?

Whey protein is commonly available in three forms:

- **Concentrate,**
- **Isolate**, and
- **Isolate with added creatine and glutamine.**

Whey concentrate is simply whey with the water removed. That leaves a powder that mixes easily for a protein shake. Most whey concentrates contain about **80%** protein, and may be the most economical form of protein for the human body to digest and use.

Whey isolate is put through a filtration process that reduces the amount of carbohydrate, lactose, and fat, providing a purer protein in the end. Whey isolate contains about **98%** protein. Those who are lactose intolerant should note that, like whey concentrate, whey isolate contains lactose.

Whey isolate with added creatine and glutamine is a premium isolate option for those seeking *greater* strength and exercise performance.

Creatine is found naturally in muscle cells. It supports energy production by increasing levels of cells' energy currency, ATP, and helps maintain healthy muscle mass.[46-48] Studies show that creatine helps build muscle and strength in explosive, short-duration activities like resistance-exercise training.[49,50]

Glutamine is abundant in muscles, but levels are reduced after prolonged and high-intensity exercise.[51-54] Glutamine encourages recovery after intense exercise, increases synthesis of energy-storing glycogen, and helps inhibit protein breakdown in muscle tissue.[55-57] It can also inhibit blood ammonia accumulation during exercise, preventing physical fatigue.[58-60]

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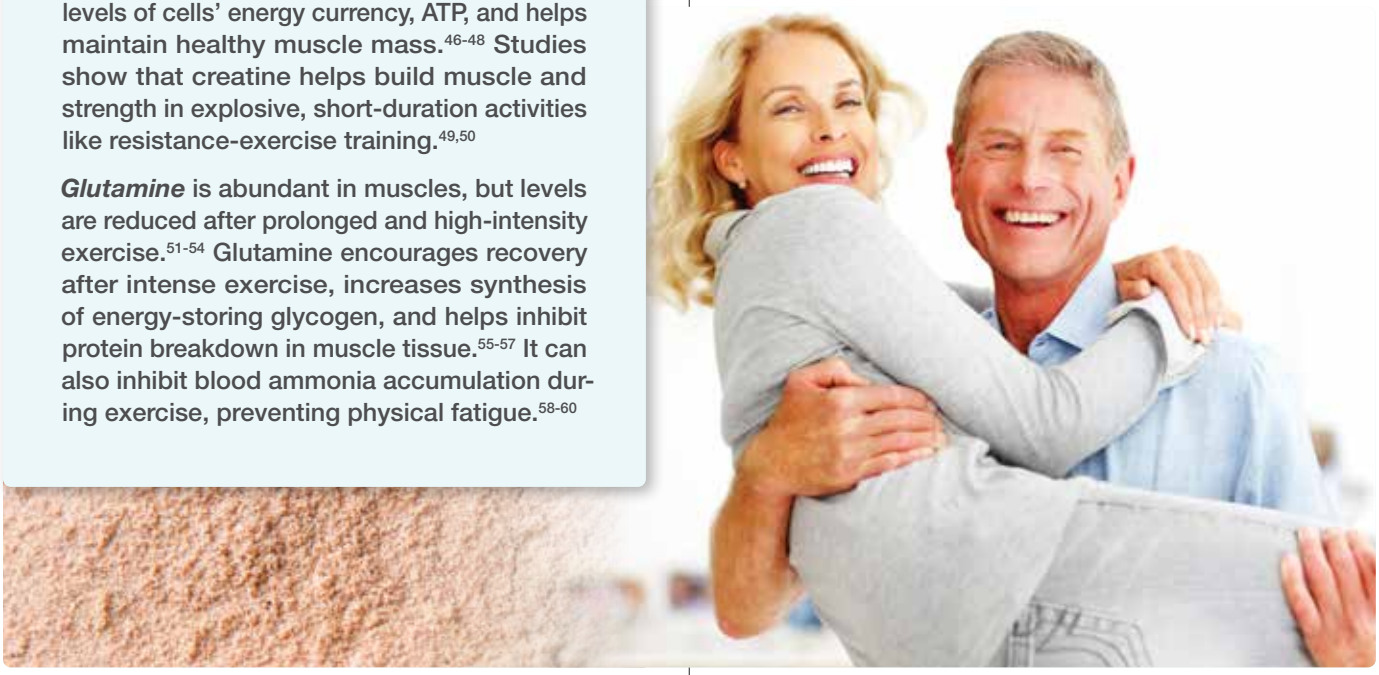

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VITAMIN C's Critical Role in Immune Health

BY JASON STERLING

We've heard it all our lives:

Vitamin C fights colds.

That's partially true.

Some **human** studies show that taking vitamin C can lessen the severity ***and*** duration of the common cold.[1]

What's **irrefutable** is the role that **vitamin C** plays in maintaining **immune function**.[2-4]

The ABCs of Vitamin C

Vitamin C is an essential nutrient in humans.[2]

Without it we die.

Humans don't internally produce vitamin C like most animals. It must be obtained from diet or other external sources.

Severe vitamin C deficiency—medically known as **scurvy**[2]—causes major health problems, including **increased susceptibility** to **infections**.[5]

Low vitamin C levels are relatively common in the United States.[2,6,7]

Diets lacking in fruits and vegetables fail to provide enough vitamin C.

Vitamin C is further depleted by smoking, illness, exposure to pollutants, and stress.[2]

As a **water-soluble** nutrient, vitamin C can't be readily stored in the body.

Impact on Infections

In the process of fighting infection, immune cells rapidly use up vitamin C.[2]

Some studies show that in common infectious illnesses, such as colds, supplemental vitamin C lessens the severity and duration of symptoms.[1]

In people with **acute respiratory infections**, like bronchitis or pneumonia, increasing oral dosages of vitamin C can reduce the severity of respiratory symptoms.[8]

The results can be dramatic. Some studies report rapid clearance on chest x-rays of patients with lung infections, following *intravenous* vitamin C treatment.[9,10]

In **pneumonia** and other serious infections, vitamin C has been shown to reduce symptoms, shorten hospital stay, and lead to more rapid normalization of markers of disease.[8,11]

Barrier Against Disease

Before viruses, bacteria, and other infectious agents can make us ill, they must invade the body, breaching **biological barriers** meant to prevent their entry.

Our skin and the linings of our respiratory and digestive tracts are protective barriers.

Vitamin C is important for the creation and maintenance of these protective-barrier tissues. It's required for the synthesis of **collagen**, a structural protein that provides strength and durability to barrier and connective tissues.[2]

Vitamin C also affects the linings of the airways in lungs, which are prone to infection. In animals with **acute lung infection**, treatment with vitamin C has been shown to restore barrier function, repairing junctions between cells in the lining of the respiratory tract.[12]

Helping Immune Cells

Vitamin C supports cells of the **immune system**, including those most directly involved in response to infections.

Neutrophils are the "first responder" immune cells against infections. They are called to infected tissues early in the course of disease. Research has shown that they play important roles in response to viral as well as bacterial infections.[13,14]

Vitamin C supports **neutrophil function** by:

- **Helping neutrophils reach an infection**. Early in an infection, neutrophils migrate to the infected tissues. Insufficient vitamin C impedes this process, making it difficult for neutrophils to find the infection.[15-17] In a study of participants with inadequate vitamin C status, daily supplementation with vitamin C resulted in a **20%** increase in neutrophil migration.[18]

- **Helping neutrophils destroy microbes**. Once neutrophils encounter an infection, they *consume and kill* infectious organisms. With vitamin C deficiency, that ability is severely impaired.[2] One study showed that increased vitamin C intake, in combination with vitamin E, enhances the ability of neutrophils to devour and kill infectious agents.[19]

After neutrophils destroy pathogens, they die off and are removed by other cells. This helps *resolve inflammation* and start the healing process. But a lack of vitamin C can cause neutrophils to die in a way that releases potentially toxic compounds, causing new inflammation and tissue damage that make disease even worse.[20,21] Preclinical studies show that adequate vitamin C inhibits this harmful process.[22]

Lymphocytes are the second most common form of immune cells. They include **B cells**, **T cells**, and **natural killer cells** (**NK cells**).

These cells are an integral part of the immune system's ability to recognize foreign invaders and mount an attack on them.

Vitamin C promotes growth, maturation, antibody production, and survival of **lymphocytes**.[23-26]

Reducing Inflammation

Excessive **inflammation** initiated by infection causes damage to tissues. Preclinical studies show that vitamin C *reduces* excessive amounts of pro-inflammatory compounds.[22,27,28]

Studies in animal models and in humans have demonstrated that oral intake of vitamin C leads to lower levels of **histamine**, a pro-inflammatory compound which causes symptoms of both infection and allergy.[17,29-31]

Fighting excessive inflammation is important in **wound healing** and recovery of tissues following injury.

By decreasing **pro-inflammatory** compounds, vitamin C helps initiate tissue-healing processes.[32]

WHAT YOU NEED TO KNOW

Vitamin C Helps Fight Infections

- **Vitamin C** strengthens **immunity** by promoting healthy barrier function to keep out pathogens and supporting optimal function of immune-system cells.
- Inadequate levels of **vitamin C** are not uncommon and can impair immune response. Requirements for vitamin C are increased when the body is fighting infection.
- ***Daily oral intake*** of vitamin C restores bodily levels and has been shown to improve the function of immune cells, supporting a healthy response to viral and other infections.
- Health-conscious people supplement with **500 mg** and sometimes much *higher* doses of vitamin C each day.

Summary

Vitamin C is an essential nutrient that supports healthy **immune function**.

Inadequate levels of vitamin C in the body impair the ability to ward off infectious disease and respond to an infection.

Increasing intake of vitamin C corrects some of these impairments. This helps strengthen barrier functions that repel infectious agents and support optimal immune-cell function.

The need for vitamin C increases with acute illness. In animal models and human clinical studies, vitamin C has been shown to reduce incidence and severity of various forms of infectious disease.

In **1970**, two-time Nobel Prize Laureate **Linus Pauling** claimed that vitamin C prevents and alleviates the episodes of the common cold.[33] Ever since, most health-conscious Americans have supplemented with **500 mg** a day (and far *higher*) of low-cost **vitamin C**.

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Reducing Cancer Risk *with* Cruciferous VEGETABLES

BY KIRK STOKEL

Roughly **1.8 million** Americans are diagnosed with **cancer** each year.

More than **600,000** people in the United States die from it annually.[1,2]

It doesn't have to be this way.

Many cancers are preventable.

Improving diet, increasing exercise, and changing unhealthy behaviors can significantly reduce risk.[3]

Studies show that *higher* intake of **cruciferous vegetables** is associated with a reduced risk for cancers.[4,5]

Ongoing research points to **anti-cancer** effects of compounds found in broccoli and other **cruciferous vegetables**.

One clinical trial showed that a specific cruciferous vegetable nutrient triggered a complete resolution of **pre-cancerous cervical lesions** in ***100%*** of women, *removing* the risk that the lesions could develop into cancer.[6]

Until recently, it was difficult to deliver these **cruciferous** nutrients into the bloodstream at high enough levels to be effective.

Scientists have found a way to maximize the **activity** of **cruciferous** compounds so that they can reach tissues throughout the body.

Cruciferous Vegetable Compounds

Cruciferous vegetables are a group of edible plants that include **broccoli**, **kale**, **green** and **red cabbage**, **cauliflower**, and **Brussels sprouts**.

They are loaded with nutrients shown to help prevent a wide variety of common disorders.

In particular, **cruciferous vegetables** have demonstrated the ability to protect cells from several processes that result in malignant transformations.[4,5]

Two cruciferous nutrients are especially well validated for their cancer-fighting properties:

1) **Sulforaphane**

2) **DIM** (3,3'-diindolylmethane).[6-8]

Findings from Johns Hopkins

In a seminal 1994 study from Johns Hopkins, rats were split into two groups. One was treated with **sulforaphane**, and one was not.[9]

All the animals were then exposed to a powerful cancer-*inducing* chemical.

The sulforaphane-treated rats developed ***39% fewer tumors*** than the untreated group. And the tumors that *did* develop progressed at a slower rate.

Other studies have produced similar findings, showing that **sulforaphane** kills cancer stem cells, slows the growth of tumors, and promotes the death of cancer cells.[10-12]

In lab and animal studies, **sulforaphane** has been associated with diminished growth of cancer cells and a reduced risk of many types of cancer including:

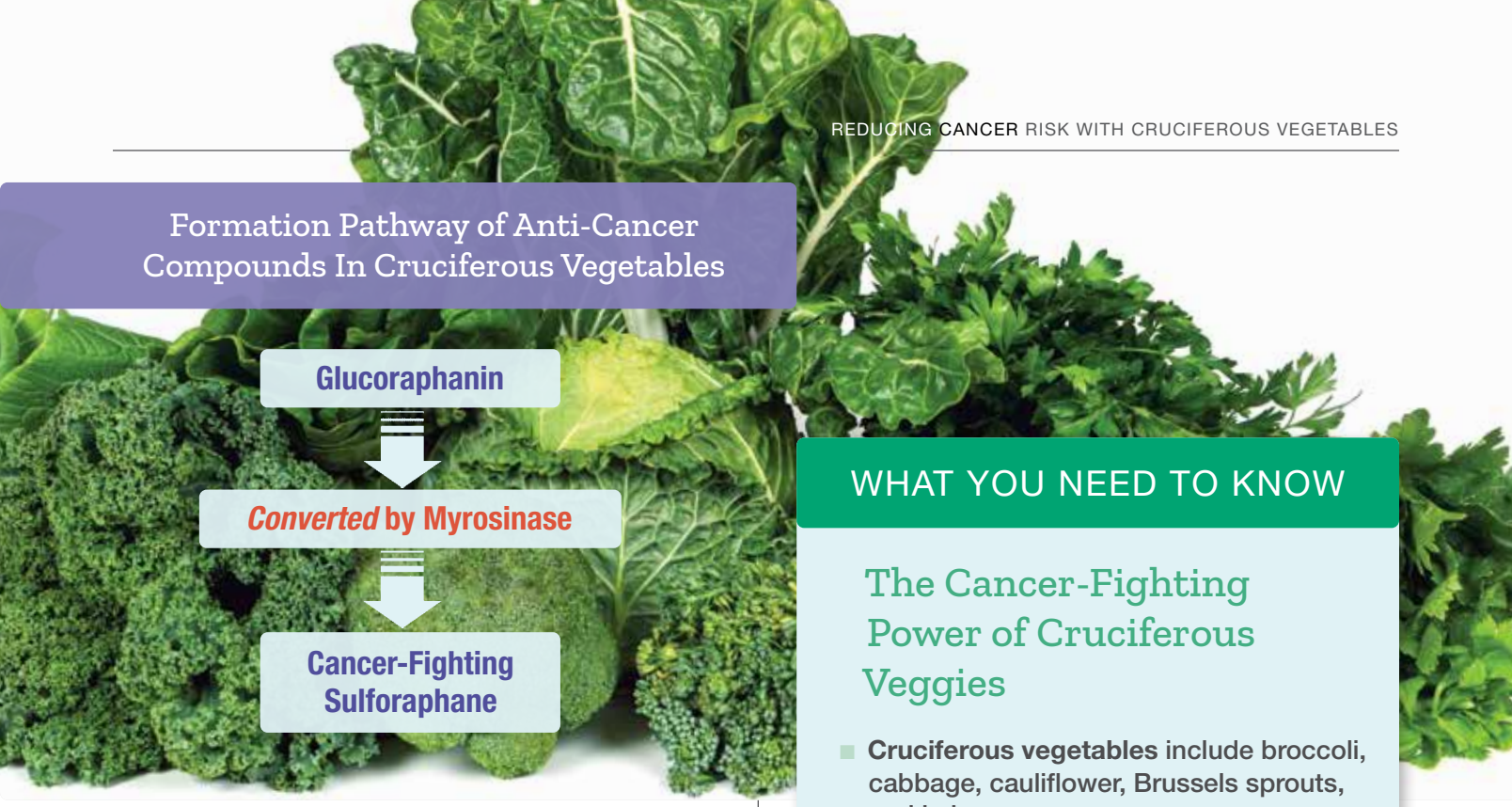
- Breast,[10-12]
- Bladder,[13]
- Lung,[14]
- Prostate,[15,16]
- Cervix,[17-19]
- Blood (leukemia),[20-22]
- Mouth,[23] and
- Brain.[24,25]

The other active compound in broccoli, **DIM**, also shows the ability to slow or even *stop* cancer cells from growing.

In one remarkable study, women with **cervical intraepithelial neoplasia**, a cervical cancer precursor, were treated with DIM.

After three to six months, ***100%*** of women receiving **200 mg** of **DIM** daily had their neoplasia ***completely resolved***, compared to **61%** of women in a placebo group.[6]

What's most striking about these cruciferous compounds is that they have shown these effects on cancer in virtually *every tissue* studied.



How Plants Create Sulforaphane

You can't get these benefits by simply popping a pill containing **sulforaphane**.

The reason is that while **DIM** is stable, **sulforaphane** is not. It degrades rapidly into **inactive** substances if it isn't quickly **absorbed**.[26]

Nature has found a way around this problem.

Sulforaphane isn't contained in cruciferous vegetables. Instead, cruciferous plants store a **sulforaphane** *precursor* called **glucoraphanin** in their cells.

In a *separate* cellular compartment, plants store an *enzyme* called **myrosinase**, that converts **glucoraphanin** into **sulforaphane**.

Only when the vegetables have been eaten and partially digested do the **glucoraphanin** and **myrosinase** mix, to form **sulforaphane**, the cancer-fighting compound.

Sulforaphane can then be absorbed through the **small intestine** before it degrades.

Science Imitates Nature

The trick for researchers was to find a similar way to deliver **sulforaphane** to the small intestine before it breaks down.

One group of scientists came up with an ingenious solution: imitate nature.

They developed a delivery system that keeps stable **glucoraphanin** and active **myrosinase** in separate compartments, just the way plants do.

WHAT YOU NEED TO KNOW

The Cancer-Fighting Power of Cruciferous Veggies

- **Cruciferous vegetables** include broccoli, cabbage, cauliflower, Brussels sprouts, and kale.
- Two cruciferous nutrients are especially well validated for their cancer-fighting properties: **sulforaphane** and **3,3'-diindolylmethane** (DIM).
- Unlike DIM, sulforaphane is unstable. It degrades rapidly if it's not absorbed.
- Scientists have found a way to package a sulforaphane **precursor** with an **enzyme** that converts it into sulforaphane ***in the small intestine***, where it's absorbed into the bloodstream right away.
- Together, sulforaphane and DIM can prevent changes that lead to cancer, stop tumors from developing and spreading, and even cause cancer cells to die off.

Taken orally, these two components meet and mix *only* in the small intestine.

That means higher levels of cancer-fighting **sulforaphane** can be achieved.

The results are striking. Scientists at Johns Hopkins found that **sulforaphane** levels from this **glucoraphanin-myrosinase** mix are **three to four times** more bioavailable (absorbable) than those created by glucoraphanin alone.[27]

How Sulforaphane and DIM Work

Sulforaphane and **DIM** have shown the ability to reduce cancer risk and malignant changes in four important ways:

- Stop deleterious **epigenetic** gene expression changes from occurring,
- Reduce or minimize cancer-promoting **chronic inflammation**,
- Fight **estrogen-driven** stimuli that encourage cancer cell replication and spread and
- Impede **pre-cancerous cells** from developing into tumors.

Stopping Epigenetic Changes

Cancer can be caused by **epigenetic** changes, the ability to "turn genes on and off."

Epigenetic changes can be described as changing gene expression via one's behavior or inadvertent exposure to outside toxins like air pollution.

By way of example, smoking cigarettes causes deleterious **epigenetic** changes that make the smoker more vulnerable to certain cancers.

Fish oil and **vitamin D**, on the other hand, have been shown to induce beneficial epigenetic changes.

These changes don't alter the DNA, but they change **expression patterns** of genes.

Research has shown that **sulforaphane** and **DIM** can reverse some of these cancer-associated changes.[16]

One example of this is that sulforaphane reverses alterations in **histone proteins** involved in the regulation of **genes**, an **epigenetic** change that can help prevent cancer formation.[28,29] This mechanism is so important, it's a target of many new cancer drugs under development.[30-32]

Suppressing Inflammation

Chronic inflammation contributes to practically *every* age-related disease—including cancer.

Our bodies have a "master switch" that regulates the signaling molecules that drive inflammation. It's called **nuclear factor-kappa B** (**NF-kB**).

Studies show that **sulforaphane** *blocks* **NF-kB**, reducing inflammation throughout the body. Along the way, sulforaphane kills **cancer stem cells** that can trigger tumor recurrence.[11,33]

Fighting Estrogen-Driven Stimuli

Certain estrogens stimulate proliferation of some existing breast and prostate cancers.[34-36]

Sulforaphane combats the potential DNA-damaging effects of estrogen, preventing the early DNA damage that leads to cancers.[37-39]

DIM helps shift the balance between two different forms of estrogen metabolites, *away* from one that promotes cancer and *toward* one that inhibits it.[40]

In women who have had **breast cancer**, human studies show that daily **DIM** shifts estrogen metabolites toward a preponderance of the healthier form.[40,41]

In men, *higher* estrogen levels are associated with prostate enlargement and cancers. Studies show DIM can prevent estrogen-induced stimulation of prostate cancer cells.[42,43]

Stop Developing Tumors in their Tracks

Sulforaphane has demonstrated the ability to *suppress* signals and enzymes that spur growth of tumors, and to *reduce* formation of blood vessels that feed them.[44-49]

DIM has also been shown to reduce new blood vessel formation in tumors and to inhibit the spread of cancer.[50]

And both compounds spur cancer cells to die off, while leaving normal, healthy cells unharmed.[51,52]

These actions prevent **pre-cancerous** cells from developing into cancer and slow the growth of existing cancer.

Summary

Cruciferous vegetables like broccoli have proven capable of slowing and even reversing the development of many types of cancer.

Research shows that many of the anti-cancer effects are due to two compounds derived from these vegetables: **sulforaphane** and **DIM**.

While **DIM** is stable and easily absorbed when taken orally, **sulforaphane** is rapidly converted to inactive compounds.

To solve this problem, scientists developed a delivery system (glucoraphanin plus myrosinase) that maximizes the amount of sulforaphane available for absorption into the bloodstream.

By separating these precursor **plant compounds**, much more **sulforaphane** becomes **bioavailable** in the small intestine. There, it can be rapidly **absorbed**, delivering higher blood levels of this beneficial (sulforaphane) compound. •

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TOCOTRIENOLS
Prevent DNA Damage *and* Combat Aging

BY JULIA CHISEN

Tocotrienols are potent forms of vitamin E that help block ***DNA damage*** associated with aging.[1-4]

DNA damage is a major degenerative factor.

Human studies demonstrate that **tocotrienols** help maintain youthful brain, bone and arterial structure, along with healthy immune function.

A review concluded that **tocotrienol** supplementation in middle-aged and elderly people can markedly reduce age-associated **DNA damage**.[3]

The Most Potent Form of Vitamin E

Tocotrienols are emerging as interesting and complex members of the vitamin E family.

Tocotrienols come in four varieties:[5]

- **Alpha-tocotrienol**
- **Beta-tocotrienol**
- **Gamma-tocotrienol**
- **Delta-tocotrienol**

These forms of **vitamin E** are different from "regular" forms of vitamin E that are called **tocopherols**.[5]

Tocotrienols generally have *higher potency* than tocopherols, and they act on a wider range of targets.

For example, **alpha-tocotrienol** prevents neurodegeneration at very small concentrations.[5]

Aging and DNA Damage Prevention

The unique structure and potency of tocotrienols make them valuable for defending aging tissues. A primary **tocotrienol** mechanism is the ability to protect against **DNA damage**, an underlying factor in most aging processes.[1]

In a randomized, clinical trial, middle-aged and older adults took either **160 mg** of mixed tocotrienols/tocopherols or a placebo for six months. By three months, there was a significant reduction in **DNA damage**, a benefit that persisted through the six-month mark.[1]

The ability to reduce DNA damage shows that tocotrienols can help slow aging at the cellular level.[3]

Because DNA damage contributes to cellular senescence, supplementing with tocotrienols represents a unique way to delay age-related decline.

Human studies have shown that tocotrienols can help lower the risk of cardiovascular disease, support bone health, and preserve cognitive function. These benefits make this unique form of vitamin E an interesting player in the fight against premature aging and disease.[3,5-10]

Cardiovascular Disease Risk Reduction

DNA damage contributes to the aging of blood vessels—a major risk factor for **heart attacks** and **strokes**.[11-13]

High levels of cholesterol and triglycerides contribute to **plaque** buildup on artery walls that causes arteries to become hard and stiff. This restricts blood flow and increases the risk of cardiovascular complications.

Tocotrienols act in numerous ways to lower the risk of cardiovascular disease. This was shown in a study of people on chronic hemodialysis for **kidney** failure.

Kidney failure patients have an extremely high risk of cardiovascular disease.

The patients took either a daily dose of **180 mg** of tocotrienols plus **40 mg** of tocopherols (traditional vitamin E) or a placebo for 16 weeks. In the supplemented group, by week 12, triglyceride levels had declined by a significant **33 mg/dL** and then dropped by **36 mg/dL** at 16 weeks. No change was found in the placebo group.[14]

Tocotrienols have also been shown to decrease arterial stiffness. When patients took **100 mg/day** and **200 mg/day** of tocotrienols, they experienced significant reductions in two measures of arterial stiffness after just two months, substantially reducing cardiovascular risk.[15]

Boosting the Aging Immune System

DNA damage directly contributes to ***immune senescence***, or a dysfunctional immune system.[16,17]

Immune senescence increases an older person's risk of infections, while also increasing the likelihood of an inappropriate immune response that can lead to excessive inflammation and autoimmune disorders.[18]

Another consequence of immune senescence is poor response to vaccines. This puts lives at risk because we rely on vaccines to prevent viral infections.

WHAT YOU NEED TO KNOW

Tocotrienols Protect Against DNA Damage

- Tocotrienols have a broad range of cell- and tissue-protecting activities.
- Tocotrienols are instrumental in preventing the DNA damage that accumulates over time and is one of the central causes of aging and disease.
- Studies show that tocotrienol supplementation slows DNA-damage-related aging and protects against heart disease, immune senescence, neurodegeneration, and osteoporosis.

A randomized, placebo-controlled trial showed that taking **400 mg** of mixed tocotrienols/tocopherols daily significantly enhanced the **immune** response to a test dose of a vaccine. This was seen through increased production of protective interferon gamma, increased production of antibodies following the vaccine, and a reduction in immune-dampening IL-6.[19]

These results suggest that tocotrienol/tocopherol supplementation can reverse major components of immune senescence, lowering the risk for preventable infections and malignancies.

Neuroprotection

DNA damage is one of the earliest detectable events in neurodegenerative diseases like Alzheimer's, Parkinson's, and ALS (amyotrophic lateral sclerosis) also known as Lou Gehrig's disease. The ***white matter lesions*** associated with dementia are also DNA damage related.[20,21]

In one study, adults with white matter lesions were randomly assigned to take either **200 mg** of mixed tocotrienols or a placebo twice daily for two years. While the lesions grew significantly in placebo recipients during that time, they remained stable in supplemented people. This demonstrates the ability of tocotrienols to help slow the progression of the disease.[22]

Animal studies have also shown that tocotrienol supplementation led to improved learning and memory as a result of reduced DNA damage.[2]

Better Bone Health

DNA damage in bone tissue promotes bone mineral loss, or **osteoporosis**, by elevating inflammatory markers and reducing the numbers of bone-forming cells.[23,24]

Animal studies have shown that tocotrienols protect bone tissue. These benefits were confirmed by a recent study of postmenopausal women (a group at high risk for osteoporosis).

This clinical trial showed that 12 weeks of supplementation with **430 mg/day** or **860 mg/day** of mixed tocotrienols decreased the excessive bone breakdown seen in osteoporosis and improved healthy bone turnover, compared with a placebo group.[25] Among the mechanisms were reductions in inflammation which, in turn, suppressed the aggressive bone resorption that typifies osteoporosis.

Anti-Aging Impact

Tocotrienols are complex nutrients with numerous interactions in cells and tissues.

This broad spectrum of actions means that tocotrienols can inhibit an array of unhealthy, destructive processes, reducing their negative impacts while potentially creating positive changes as well.

The following are six features of tocotrienols that contribute to their anti-aging properties:

- **Tocotrienols reduce oxidative stress.** Tocotrienols are potent antioxidants that protect against chemical- and radiation-induced DNA damage.[1,2,26-28]

- **Tocotrienols reduce the activity of HMG-CoA Reductase.** This *enzyme* participates in chemical reactions that play a role in cholesterol production inside the body, in cancer, and in osteoporosis.[8,28-30]

- **Tocotrienols enhance immune function.** They elevate production of signaling molecules that recruit immune cells and instruct them in their duties, as well as interferon-gamma, a signaling molecule that enhances anti-tumor surveillance.[31]

- **Tocotrienols reduce inflammation.** They act by suppressing major pro-inflammatory signaling pathways, including NF-kappaB, called the "master inflammation regulator."[8]

- **Tocotrienols reduce unwanted new blood vessel formulation.** This is an important way to fight cancer (which needs new vessels for nutrition) and cardiovascular disease (in which tiny, new blood vessels that grow inside of atherosclerotic plaques contribute to the growth of those plaques).[32] Tocotrienols fight the kind of new blood vessel formation that may contribute to cancer and heart disease.[10,33]

- **Tocotrienols boost mitochondrial energy production.** This property has value in energizing heart and brain tissues during aging.[34]

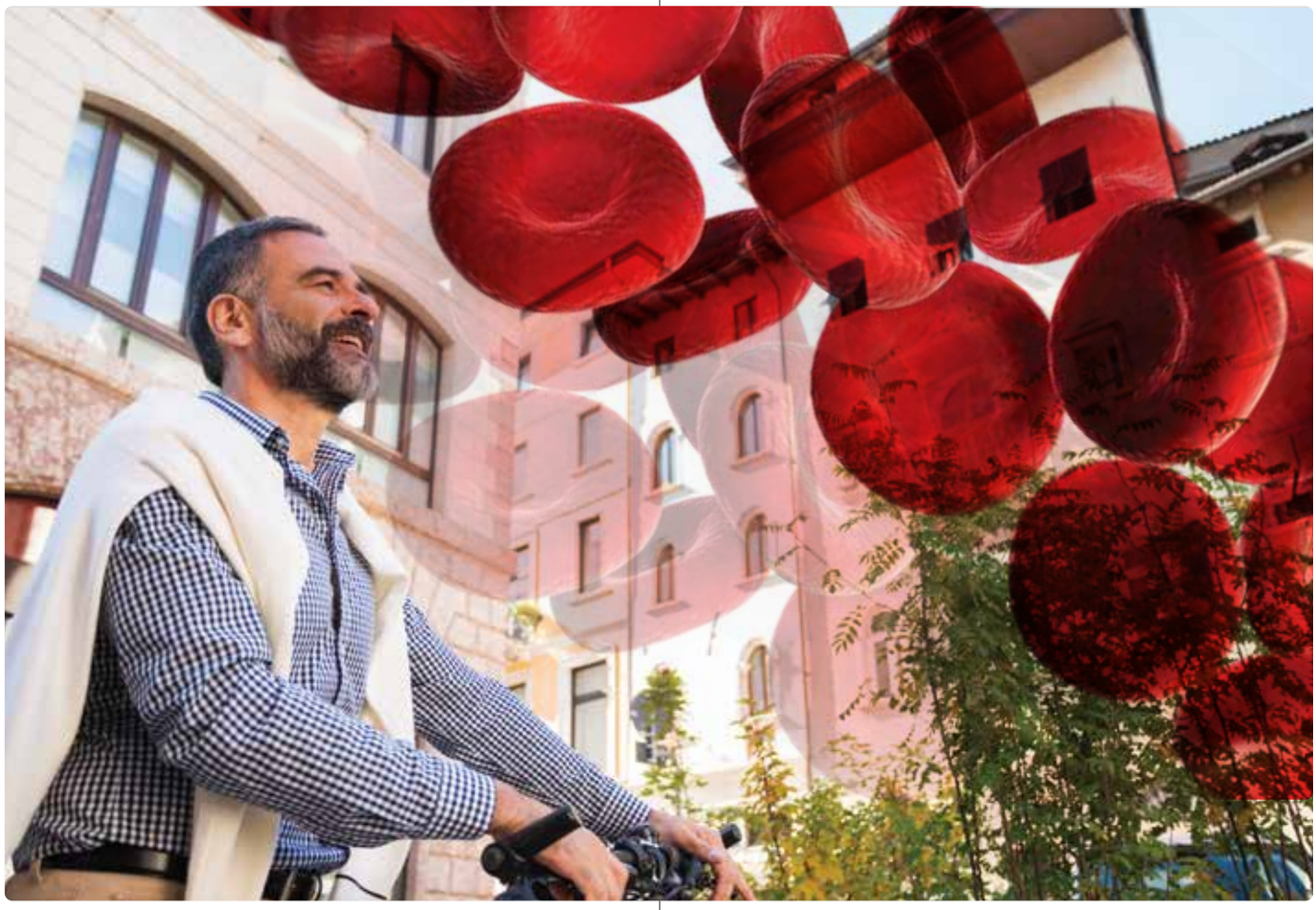
Summary

DNA damage is a common underlying factor in numerous age-related disorders.

Studies show that ***tocotrienols*** can fight DNA damage and slow the aging process in tissues throughout the body.

In human studies, tocotrienols have now demonstrated benefits in regard to DNA-damage-related aging, heart disease, immune regulation, neuroprotection, and bone health.

Formulations of mixed tocotrienols are available as supplements for those seeking this age-decelerating nutrient. •



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The Vegetarian Silver Spoon

Originally published in 1950, *The Silver Spoon* cookbook soon became a global best-seller, featuring traditional, home-cooked, Italian dishes.

Numerous offshoots have been published since then, but the recently published *The Vegetarian Silver Spoon* is the first collection of strictly vegetarian dishes.

With more than 200 recipes for healthy, meat-free Italian dishes, *The Vegetarian Silver Spoon* includes ingredients that have come to define Italian cuisine, plus contemporary additions like spelt and buckwheat.

Each recipe is conveniently labeled as being vegetarian, vegan, gluten-free, dairy-free, 30 minutes or less, and five ingredients or less.

Here, ***Life Extension***® features a recipe from *The Vegetarian Silver Spoon* that showcases both the variety and simplicity of traditional Italian, home-style cooking.

—LAURIE MATHENA

Stuffed Cabbage with Buckwheat and Pumpkin

Preparation Time: 20 minutes

Cooking Time: 1 hour

Serves: 4

½ cup (120 ml) extra virgin olive oil

1½ cups (250 g) buckwheat, rinsed

7 oz (200 g) peeled pumpkin, cut into small cubes

1 clove garlic, finely chopped

Handful of parsley leaves, chopped

⅔ cup (80 g) chopped walnuts

Scant 1 cup (200 mL) vegetable stock

1 small savoy cabbage

1 small red onion, very thinly sliced

Salt and black pepper

In a medium saucepan, heat 2 tablespoons of the olive oil over medium heat. Add the buckwheat and toast, stirring continuously, for 2 to 3 minutes. Add 2½ cups (600 mL) boiling water, reduce the heat to low, and cook for 20 minutes.

In a large frying pan, heat 2 tablespoons of the oil over medium heat. Add the pumpkin, garlic, a pinch of salt, and a scant ½ cup (100 mL) boiling water. Cook until the pumpkin is tender, then transfer it to a medium bowl. Mash the pumpkin with a fork and add the buckwheat, parsley, walnuts, a pinch of salt, and some pepper. Stir well to combine.

In a small saucepan, bring the stock to a boil.

Bring a large pot of salted water to a boil. Discard the outer leaves from the cabbage. Pull off 12 leaves, put them in the boiling water, and blanch for 2 minutes, then drain them and cut out the tough central ribs.

Spread the cabbage leaves out on your work surface (work in batches, if necessary). Divide the buckwheat mixture among the cabbage leaves, placing it in the center of the leaves and folding the leaves over the filling to make small parcels.

In a large nonstick frying pan, heat the remaining ¼ cup (60 mL) oil. Add the onion and 2 tablespoons of the hot stock. Arrange the stuffed cabbage leaves in the saucepan, then add the remaining stock. Cover and cook for 25 minutes, until the cabbage leaves are translucent and the filling is heated through, then serve.

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Marigold extract (packed with carotenoids lutein and zeaxanthin), standardized Gotu kola extract and always-popular *Bacopa monnieri* extract have been clinically studied to encourage mental sharpness, improve learning and retention scores and promote faster neural processing speeds.[1-5]

This formula is for anyone, regardless of age. So, try our NEW Quick Brain Nootropic formula. And think faster on your feet!

1. *Front Aging Neurosci.* 2017;9:254.
2. *J Int Neuropsychol Soc.* 2018;24(1):77-90.
3. *Nutrients*. 2017;9(11).
4. *J Ethnopharmacol.* 2008;116(2):325-32.
5. *Psychopharmacology (Berl)*. 2001;156(4):481-4.

Does your multivitamin measure up?

Two-Per-Day beats Centrum® in 10 ways!*

Get The Maximum Potency From Your Multivitamin!

Life Extension's **Two-Per-Day** formulas are the highest potency multivitamins. Compared to **Centrum®** Silver® Adults 50+, **Two-Per-Day** provides:

Centrum® Can't Compete

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

Life Extension's **Two-Per-Day** contains superior forms of nutrients such as **5-MTHF** that is almost **7 times** more **bioavailable** than **folic acid**. These **bio-active** nutrients provide the body with greater biological **activity**, which is especially important as people age.

Two-Per-Day Capsules
Item #02314 • 120 capsules
(Two-month supply)

Two-Per-Day Tablets
Item #02315 • 120 tablets
(Two-month supply)

These products are available at fine health food stores everywhere.

*Formula compared to Centrum® Silver® Adults 50+.

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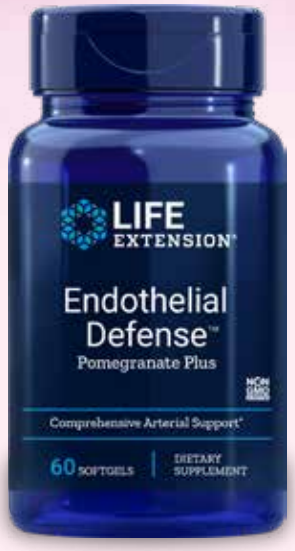
Triple-Protect Your Vascular System

The inside lining of your blood vessels is called the vascular endothelium. It's so important to your health, we created a formula exclusively to support and promote it.



Protect endothelial cells critical to cardiovascular health.

Pomegranate—protects arteries from oxidation with free-radical-quenching polyphenols.

Extramel® melon concentrate—encourages superoxide dismutase production, a naturally occurring antioxidant.

Cardiose®—promotes circulatory health with hesperetin extracted from sweet orange peels.

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