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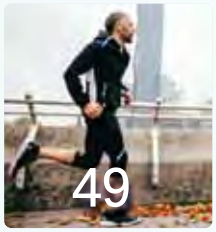

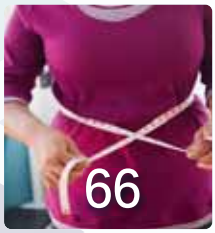

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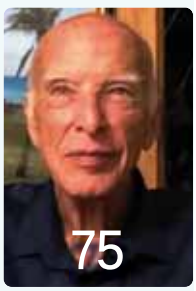

LIFE EXTENSION®

The Science of a Healthier Life®

LifeExtension.com February 2021

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

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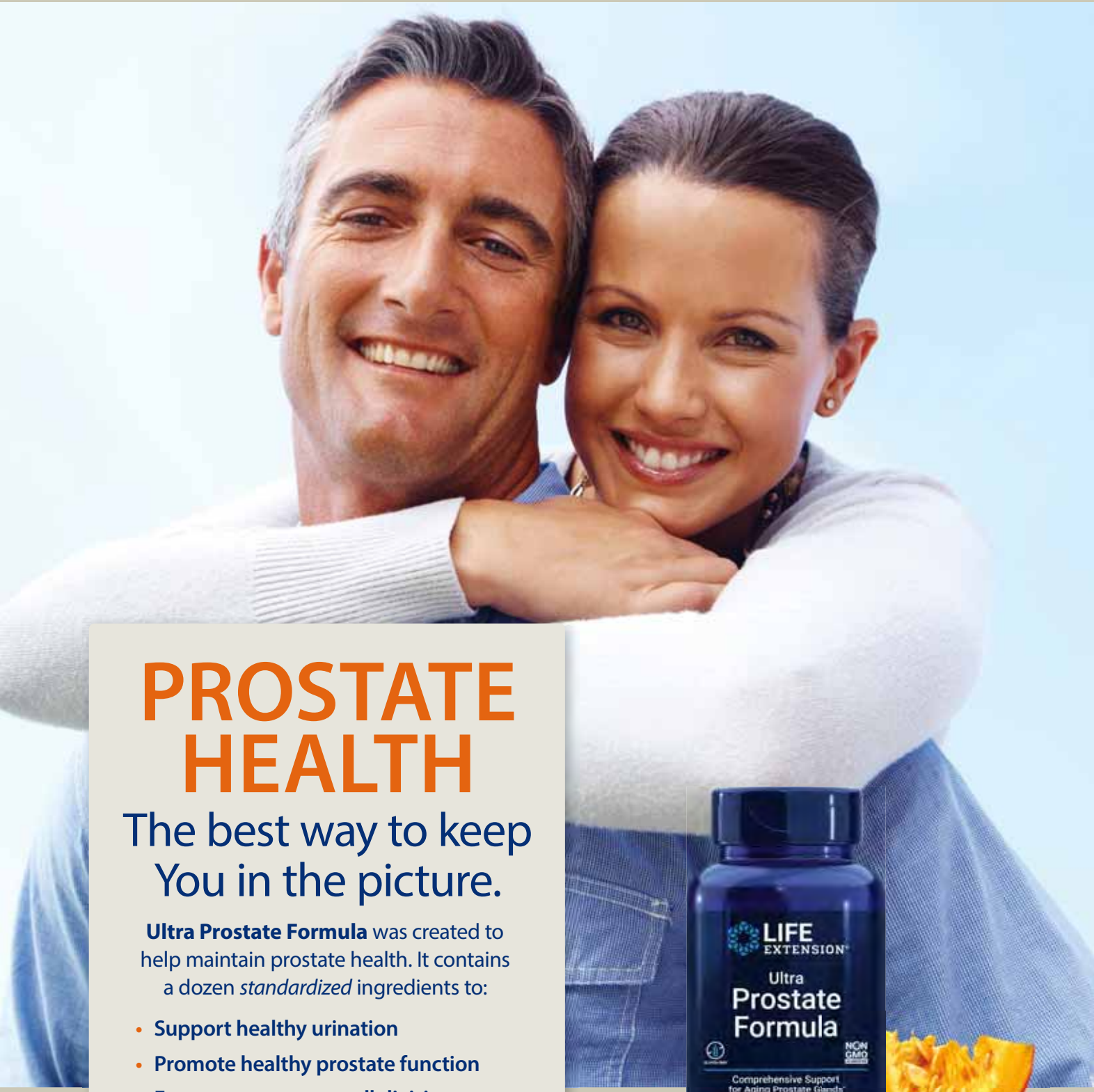

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EXPEDITING MEDICAL PROGRESS

WILLIAM FALOON

*In **2020**, rapid advancements occurred in our understanding of **immune** function.*

But what about those who perish from **cancer**, **diabetes,** and **dementia?**

Why not make **heroic** attempts to better manage these diseases as well?

I first learned about the havoc that **senescent cells** inflict on our aging bodies in the **1990s**.

Scientists made it clear that for meaningful **longevity improvements** to happen, the senescent cell **burden** had to be reduced.

Until recently little could be done.

In 2016, **Life Extension**® learned of a flavonoid found in **strawberries** and **apples** that demonstrated profound **senolytic** effects.

The name of the flavonoid is **fisetin**. The challenge was that fisetin is rapidly metabolized in the **digestive tract**, leaving little for **absorption** into the blood.

Many years were spent developing a method to enhance fisetin's **oral bioavailability** in order to obtain its **systemic** benefits.

A low-cost orally *absorbable* **fisetin** supplement has finally arrived.

Five **clinical trials** are now recruiting people to study whether **fisetin** can combat some of the most difficult health challenges aging **humans** confront.[1]

I sincerely regret **delays** in moving **lifesaving** therapies forward. Each day an effective method is postponed means needless loss of life.

This month's issue reveals validated methods to promote healthy **human lifespans**.

An article on **page 49** of this month's issue provides fascinating evidence about the **disease prevention** possibilities of both **intermittent fasting** and **caloric restriction**.

The easiest way to accomplish this is to not ingest anything except water, tea, or black coffee for about **16 hours** on most days.

I've been following this strategy and advocating it for many years. A review article published in the ***New England Journal of Medicine*** opened the eyes of even conventional doctors to this health-promoting science.[2]

Intermittent fasting induces healthy biological responses throughout our aging bodies.

Up until now, most people were challenged to garner these benefits without feeling hungry most of the time.

Obtain Some Fasting Benefits with Fisetin

Consuming fewer calories has long been associated with reduced cancer risks.

Fisetin has been the subject of much scientific interest for its potential to thwart **cancer**.

Fisetin is a plant flavonoid that selectively removes **senescent cells**, but research shows it does far more.

The **anti-cancer** effects of **fisetin** have been attributed to several properties, including its ability to induce cellular **apoptosis** and **autophagy**.[3-12]

Apoptosis is the programmed elimination of cells, including those that are older and mutated.

Intermittent fasting or calorie restriction promotes **apoptosis** and **autophagy** (removal of waste products inside cells), but so does **fisetin**.

Anti-Cancer Mechanisms

Instead of undergoing apoptosis, **cancer cells** override normal processes that remove damaged cells thereby allowing the cancer to proliferate out-of-control.

Fisetin helps restore normal **apoptotic** processes to help control a wide range of malignant abnormalities.

Autophagy can be described as "cellular housekeeping."

In healthy cells, autophagy is used to clear out accumulated **debris** inside of cells. This helps to facilitate normal cell division.

Time-restricted eating and **caloric restriction** induce these kinds of beneficial changes (apoptosis + autophagy) and may reduce risk of cancers, diabetes, dementia, and a host of metabolic disorders. Fisetin may induce similar benefits.

Curtailing Metastasis

Cells that escape a primary tumor migrate throughout the body and establish metastatic colonies that are often the cause of death in cancer patients.

Fisetin blocks *signaling* factors that enable cancer cells to spew out protein-degrading *enzymes* that enable invasiveness and eventual metastasis of tumor cells.[5,13]

In a laboratory study using triple negative **breast cancer** cells, fisetin reduced migration by **76%** and inhibited metastasis.[14] The effects were likely due to fisetin interfering with several pathways involved in **metastasis**.

Impeding Angiogenesis

Malignant cells develop their own blood supply to feed their rapid proliferation.

Angiogenesis refers to the formation of new blood vessels, including into a tumor bed.

Fisetin *inhibits* angiogenesis by disrupting *signals* that tumor cells use as a "switch" to promote new blood vessel growth.[15]

One lab study found that fisetin inhibited **vascular endothelial growth factor** (VEGF) growth up to **92%** in human umbilical vein endothelial cells.[4]

Mouse studies show **fisetin** decreases angiogenesis and lung tumor growth.[3]

Suppressing Inflammation

In preclinical studies, fisetin has been shown to inhibit many **inflammatory** factors such as TNF-alpha, IL-1 beta, IL-6, and IL-8.[16,17]

In a rat model of primary liver cancer, the rats treated with **fisetin** experienced a normalization of TNF-alphaα and IL-1 beta. These inflammatory cytokines are involved in liver cancer pathology. Fisetin-treated rats had a regression of neoplastic lesions in the liver in this study.[18]

In a randomized controlled clinical trial, 37 patients with colorectal cancer undergoing chemotherapy were given either **fisetin** or **placebo** for seven weeks. At the end of the trial, plasma levels of IL-8, C-reactive protein, and a protein-degrading enzyme (MMP-7) were significantly reduced in the **fisetin** group, but not in the **placebo** group.

The authors suggest that fisetin can improve the inflammatory status in colorectal patients, making it a potential complementary therapy.[19]

Further studies are necessary to fully elucidate the usefulness of fisetin as a cancer adjuvant.

Neuroprotection

Fisetin has been studied for its brain-protective properties, which stem partially from its **anti-inflammatory** effects.

In the context of brain diseases, fisetin has been investigated in Alzheimer's, Parkinson's, and Huntington's, as well as in models of stroke, neurotoxicity and traumatic brain injury.[20,21] Fisetin has displayed promise in many of these areas, and showed some benefit in a clinical trial with **stroke** patients.[22]

As it relates to **brain regeneration**, fisetin appears to promote neurite outgrowth and brain cell differentiation.[23] In multiple animal studies, fisetin improved learning, memory, and cognition.[24,25]

In a mouse model of **Alzheimer's** disease, fisetin reduced ***beta-amyloid*** deposits and retarded the process by which tau proteins become toxic.[26] Fisetin-treated mice in this study had improved memory and diminished neuroinflammation.[27]

In a mouse model of **amyotrophic lateral sclerosis** (ALS), mice treated with fisetin had improved survival and redox balance, and reduced motor impairment, compared to control mice.[28]

In another study, mice with **intracerebral-hemorrhage**-induced brain injury were treated with fisetin, which lowered multiple indicators of brain trauma and neuroinflammation, including reducing levels of **inflammatory cytokines.** This suggests the brain injury was diminished.[29]

Fisetin prevented behavioral and biochemical changes in a rat model of **Parkinson's** disease. The treated rats experienced improvements in motor function and dopamine levels, indicating fisetin could have a favorable influence on the pathogenesis of Parkinson's disease.[30]

Preventing Stroke Damage in Humans

A clinical trial using fisetin was conducted in 192 patients who had experienced an ischemic **stroke**. The patients' onset-to-treatment time had been carefully recorded, as stroke treatment is most effective when administered **within three hours** of symptom onset.

The patients were treated with the standard of care—an IV injection of the clot-dissolver drug **tissue plasminogen activator** (tPA)—along with either placebo or **100 mg fisetin** in the **IV fluid**.

After the initial emergency care, patients continued with **placebo** or **fisetin** for **seven days**.

There was no difference in treatment outcome between placebo and fisetin among the patients who were treated between **zero and three hours** after onset of stroke symptoms.

When onset of symptoms to treatment time was **three to five hours**, however, there was improvement in the **fisetin** group compared to the **placebo** group with the same delayed (three to five hours) treatment time.[22]

Interestingly, the patients in the **three to five hour** *delayed* treatment group who received fisetin experienced favorable neurological scores almost **identical** to those who had received standard treatment within **three hours**.

The researchers concluded that **fisetin** may be a valuable supplement to clot-dissolving drug treatment for stroke patients, especially in those with delayed treatment after symptom onset.

Diabetic Complications

Diabetic complications such as eye disorders, neuropathy, kidney impairment, and cardiomyopathy may be improved with fisetin administration.

In a mouse model of diabetes, fisetin slowed the advancement of **cataracts**.[31] Fisetin also stopped the development of painful **neuropathy** in diabetic mice.[32]

Diabetic rats given fisetin experienced improved body weights and reduced blood glucose and A1c. Fisetin-treated rats had improved lipid profiles and significant lessening of diabetes-induced heart damage.[33]

In obese mice fed high-fat diets, **fisetin** protected **kidneys** from pathologic alterations and improved kidney function. Fisetin also decreased **inflammation** in kidneys as demonstrated by reduced levels of TNF-alpha, IL-6, IL-1 beta, and IL-18.[34] These results indicate that fisetin may be beneficial in diabetic kidney disease.

Human Clinical Trials

There are several active clinical (human) trials underway to determine the effects of fisetin,[1] including one in patients with advanced **kidney** disease, particularly diabetic kidney disease.[35]

These studies will measure changes in inflammatory markers, stem cell function, kidney function, and more.

Additional clinical trials with diabetic participants that measure glucose levels, insulin resistance, and HbA1c will help determine the role of **fisetin** in preventing and treating diabetes and its complications.

"Obesity" Control Switch

Fisetin may play a role in regulating obesity by preventing fat-cell production via suppression of **mTOR** signaling.

When mice were fed a high-fat diet, fisetin attenuated the increase in body weight and white adipose tissue accumulation.[36]

Other animal studies indicate that fisetin may be helpful in addressing another issue of obesity: fatty liver.[37-40]

In one study, mice were given a high-fat diet to induce fatty liver. The fisetin-treated mice had *decreased* body weight and lipid accumulation in the liver.[40]

What Has Scientists Most Excited?

What got **Life Extension®** excited about **fisetin** is its ability to act as a *targeted* **senolytic**.

Senolytic compounds selectively remove **senescent cells** from our aging bodies and have demonstrated remarkable health and longevity improvements.

Currently, the best proven senolytic protocol uses a combination of the cancer drug **dasatinib** with the flavonoid **quercetin**.

It is possible that dasatinib could have some off-target effects, such as removing a few healthy cells in the process of purging toxic senescent cells. Dasatinib is nonetheless currently the best documented senolytic agent when combined with quercetin.

With the advent of **bioavailable fisetin**, it may no longer be necessary to use dasatinib to reduce the senescent cell burden.

In a panel of 10 flavonoids tested in progeroid mice, **fisetin** was the most potent **senolytic**.[41]

Progeroid mice suffer accelerated aging, just like humans afflicted with progeria. Supplementation with fisetin in progeroid mice resulted in reduced senescent markers in fat, spleen, liver, and kidney.[41]

Fisetin has also been shown, in preclinical models, to lower harmful secretions from **senescent cells,** a phenomenon called the **"senescent associated secretory phenotype"** (SASPs). This finding of lowered SASP markers indicates that senescent cells were either cleared (meaning fisetin removed senescent cells) or had their senescence reversed.[41-43]

In naturally aged mice (roughly equivalent to **75 years** in humans), supplementing the diet with fisetin:[41]

- Restored tissue homeostasis,
- Reduced age-related pathologies, and
- Extended lifespan.

Similar lifespan-enhancing effects have been seen in other organisms like yeast and flies.[44,45]

It has been suggested that such effects may be due to fisetin inhibiting the **mTOR pathway** and other deleterious factors involved in aging.[44,46-48]

Researchers are conducting clinical trials using very high doses of regular fisetin (not a new bioavailable form) to measure changes in senescent cell burden, inflammation, frailty, and other indicators.[49]

We look forward to findings as more clinical studies about fisetin are published.

What You Might Consider

The **senolytic** properties of **fisetin** make it appropriate to use in a modest daily dose of **8 mg** in its new **bioavailable** form, which is equivalent to about **200 mg** of regular fisetin.

Fisetin has demonstrated favorable biological effects in preclinical studies, including preventing and suppressing inflammation, regulating cell proliferation, protecting neurons and controlling mTOR.

These benefits are analogous to what happens in response to **intermittent fasting**—a proactive health and longevity measure that I urge you to consider as a New Year's resolution.

I eat my last meal around 3 a.m., sleep eight hours and then wake up and immediately begin my 10+ hour workdays. This enables me to not eat anything for 16 or more hours most days.

I augment this **intermediate fasting** with phytoextracts from green tea and other plants, NAD^+ boosters, metformin, and now **bioavailable fisetin**.

At less than **33 cents** a day, fisetin is an exciting and affordable new plant extract.

Concept of Daily Senolysis

Young, healthy bodies meticulously remove senescent cells **every day.**

With age, the **senescent cell burden** creates a snowball effect of mounting health problems and inability to remove senescent cells until life is no longer sustainable.

Stated in another way, accumulated senescent cells reduce their own removal rate.[50]

With the advent of **targeted senolytics** like **bioavailable fisetin**, daily use may be considered, or perhaps weekly as described in the box on the next page.

Do You Still Need Other Senolytics?

Most of you are following some sort of senolytic protocol that may involve:

- Two-day-a-week fasting (not eating **anything** for two days a week or ingesting only **500-600 calories** two days a week) or time-restricted eating (fasting 14-18 hours most days) and/or
- Dosing of dasatinib + quercetin one or more times a year and/or
- Weekly dosing of black tea theaflavins + quercetin + apigenin.

Fisetin is generating tremendous interest among researchers who specialize in anti-aging science.

For the first time people can obtain it in bioavailable form as opposed to taking over **1,400 mg** and hoping enough is transported into your bloodstream.

For those who want to continue with an intermittent senolytic program, taking seven (**8 mg**) capsules once a week of **bioavailable** fisetin along with a combination formula providing black tea theaflavins + quercetin + apigenin is an option.

You may also take the daily bioavailable fisetin dose for its other benefits and then continue with weekly black tea theaflavins + quercetin + apigenin.

Studies are planned for using bioavailable fisetin on differing dosing schedules to ascertain the ideal protocol for removing senescent cells and reducing the "senescent associated secretory phenotype" (SASPs).

While the data on **dasatinib** are compelling, some longevity enthusiasts who have used it reported experiencing mild flu symptoms or GI upsets, whereas **fisetin** does not cause these side effects.

I look forward to results from human trials to identify the optimal senolytic protocol for aging persons to follow. This may involve all known senolytic compounds based on individual response rates as measured by the "senescent associated secretory phenotype," skin punch measures of senescent fibroblast cells, or other senolysis-measuring methods that are still being explored.

In This Month's Issue

Those who follow healthy lifestyles underestimate the degree of **bone loss** that occurs with normal aging. The article in **page 26** describes what Japanese physicians are using to improve **bone density** and reduce **fracture risk**.

As the **obesity epidemic** worsens, more Americans are succumbing to **heart attack** and other metabolic disorders. The article on **page 49** reviews data on how **time-restricted eating** may lessen the impact of the unhealthy dietary patterns that too many of us engage in.

The article on **page 58** describes recent findings on how a **plant extract** most of you supplement with can improve **cardiac function**.

Please know that I work around-the-clock to expedite **clinical trials** aimed at reversing **biological aging** in older individuals. Your long-standing support enables me to fund a full-time program to transform **human research** into affordable reality.

For longer life,

William Faloon, Co-Founder
Life Extension Buyers Club

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FISETIN

Enhanced Bioavailability

Fisetin, a flavonoid found in strawberries and apples,[1,2] is currently being studied as a **senolytic** in humans.[3]

In preclinical studies, fisetin:

- Mimics the effects of **calorie reduction**[4]
- Supports activation of **longevity proteins**[4-8]
- Extends the lifespan of mice by approximately **10%**[9]
- Removes aging **senescent** cells through **senolytic** action[9]
- Suppresses **mTOR** activation[10]

Fisetin is poorly *absorbed* due to its breakdown in the small intestines.

Bio-Fisetin solves this problem by enclosing **fisetin** with a compound from the fenugreek herb.

The result of a **human** trial showed **bioavailability** of this new **fisetin** compound increased up to ***25 times*** compared to fisetin by itself.[11]

Just one capsule daily of **Bio-Fisetin** helps manage **senescent cells** and may support overall longevity.

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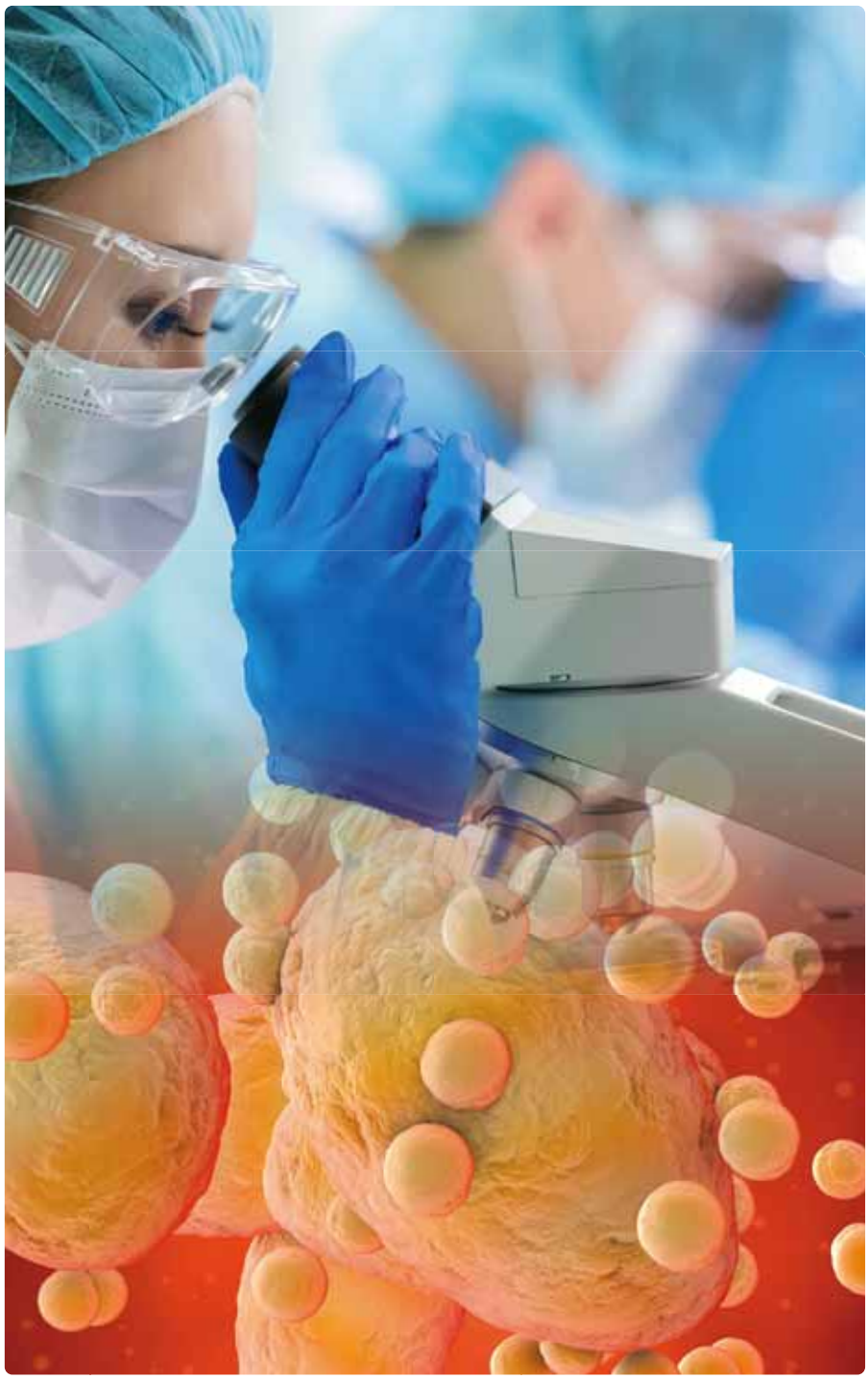
In the News



Caloric Restriction Protects Against Liver Disease, Animal Study Suggests

Consuming fewer calories has a protective effect against developing hepatocellular carcinoma (primary liver cancer) associated with hepatitis C virus infection, and nonalcoholic fatty liver disease, according to a rodent study published in the journal *Liver Cancer*.*

The study used mice with the liver cancer core gene that spontaneously develop fatty liver and tumors. For 15 months, the animals were given either a control diet that allowed them to eat as much as they liked, or a diet that contained **30%** fewer calories than the control.

At the end of 15 months, animals that received calorie-restricted diets had fewer and smaller liver tumors, less liver oxidative stress, lower inflammation, downregulation of pro-cancer mediators, increased autophagy, as well as other improvements, compared to the control group.

Editor's Note: "Recently, worldwide increases in obesity and metabolic syndrome have raised the prevalence of primary liver cancer derived from nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH), indicating a close relationship between overnutrition and liver tumorigenesis," the authors stated.

* *Liver Cancer.* 2020 Sep;9(5):529-548.

Why Does Being Overweight or Obese Increase Alzheimer's Risk?

Numerous studies have shown that obesity increases the risk of Alzheimer's disease, but they haven't identified why the connection exists. A recent brain-imaging study published in the *Journal of Alzheimer's Disease* has identified an underlying connection.*

Researchers analyzed over 35,000 brain scans of more than 17,000 individuals, using SPECT (single-photon emission computerized tomography). They found that people with a *higher* body mass index had decreased blood flow to the brain. The subjects ranged in age from 18 to 94.

Decreased brain blood flow is the number one brain-imaging predictor of Alzheimer's disease.

As people progressed from overweight to obese to morbidly obese, reduced blood flow progressively worsened. In addition, the areas of the brain impacted by reduced blood flow were those especially vulnerable to Alzheimer's disease.

This is one of the largest brain imaging studies, until now, tying obesity to brain dysfunction.

"This study shows that being overweight or obese seriously impacts brain activity and increases the risk for Alzheimer's disease as well as many other psychiatric and cognitive conditions," said Dr. Daniel G. Amen, lead author of the study, and founder of Amen Clinics.

Editor's Note: "Overall, we have found a strong set of relationships between being overweight and obese and brain hypoperfusion across a large adult cohort spanning young adults to late life. The persistence of these abnormalities despite adjusting for demographic and psychiatric factors further highlights the need to address obesity as a target for interventions designed to improve brain function, be they AD prevention initiatives or attempts to optimize cognition in younger populations," the authors concluded.

**J Alzheimers Dis*. 2020;77(3):1331-1337.

Greater Cruciferous Vegetable Intake Associated with Less Aortic Calcification

Research findings reported in the *British Journal of Nutrition* reveal an association between increased intake of Brussels sprouts, broccoli, cabbage, and other cruciferous vegetables, and less extensive abdominal aortic calcification (AAC) in older women.*

Conducted by researchers from the University of Western Australia, the study included 684 women, with a mean age of 75, who had enrolled in the Calcium Intake Fracture Outcome Study in 1998. Responses to dietary questionnaires administered upon enrollment provided information about cruciferous vegetable intake. Aortic calcification was categorized as extensive or not extensive based on imaging obtained during 1998–1999.

A correlation was observed between greater cruciferous vegetable intake and a reduction in AAC. Women whose intake of the vegetables was more than **44.6 grams** per day (the equivalent of ¼ cup of steamed broccoli or ½ cup of raw cabbage, for example) had a **46%** lower adjusted risk of extensive AAC, compared to those whose intake was less than **15 grams** daily.

Total vegetable intake, including other types of vegetables, was not related with risk.

"This study strengthens the hypothesis that higher intake of cruciferous vegetables may protect against vascular calcification," the authors stated.

Editor's Note: "One particular constituent found abundantly in cruciferous vegetables is vitamin K which may be involved in inhibiting the calcification process that occurs in our blood vessels," said lead author Dr. Lauren Blekkenhorst.

* *Br J Nutr.* 2020 Jul 17.

Cardioprotective Benefits Found with Omega-3 Supplements

An updated meta-analysis published in *Mayo Clinic Proceedings* expands on an earlier one, supporting a cardioprotective role for supplementation with the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).*

This meta-analysis included 40 randomized controlled trials with a total of 135,267 participants.

Dosages of omega-3 used in the studies ranged from **400 mg** to **5,500 mg** per day.

Supplementation with EPA + DHA was associated with a:

- **13%** lower risk of heart attack,
- **10%** lower risk of coronary heart disease events,
- **35%** lower risk of fatal heart attack, and
- **9%** lower risk of coronary heart disease mortality.

Editor's Note: When the impact of omega-3 dosage was examined, higher doses were more protective against the risk of cardiovascular disease events and heart attack than lower amounts.

* *Mayo Clin Proc.* 2020 Sep 17.

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Reference

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

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

CAUTION: If you are taking glucose-lowering medication, consult your healthcare provider before taking this product.

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CAUTION: Individuals consuming more than 50 mcg (2000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.

High-Dose Vitamin K2 Builds New Bone

BY MICHAEL DOWNEY

Osteoporosis is astonishingly common in men and women.

Roughly **50%** of American women and **25%** of American men age 50 and older will suffer a **fracture** due to this condition.[1]

These bone breaks are a leading cause of disability. Within a year of suffering a hip fracture, up to **20%** of patients over 50 ***will die***.[2]

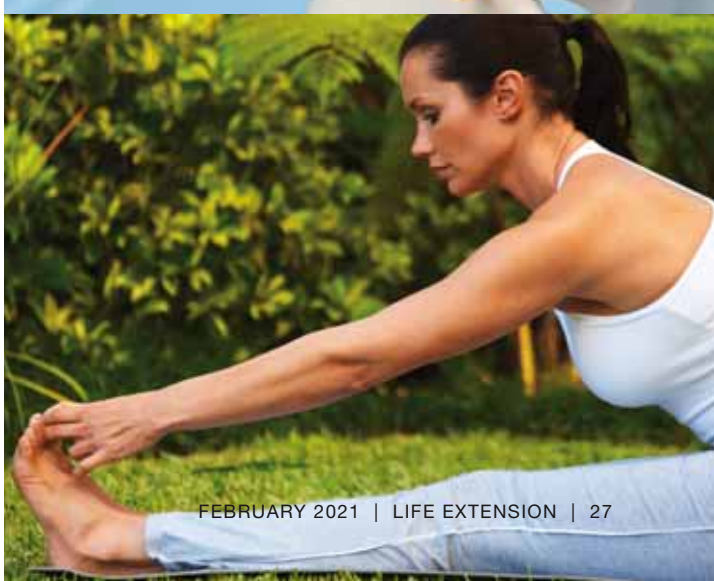
For decades, doctors in Japan have been using **high doses** of **vitamin K2** as a prescription drug to prevent ***bone loss*** and protect against **fractures**.[3]

It is now available in the U.S. *without* a prescription.

Clinical trials have demonstrated that **45 mg** of **vitamin K2 (menaquinone-4)** helps to:[4-11]

- Slow bone loss,
- Reduce fracture risk, and
- Build *new* bone.

A two-year study of older osteoporosis patients showed that high-dose vitamin K2 cut the number of people suffering a **vertebral** fracture by **half**.[11]



The Danger of Osteoporosis

Osteoporosis is a condition that causes bones to become weak, brittle, and prone to **fractures**. After suffering one fracture, the risk of future breaks increases by **86%**.[2]

Fractures of the **hip** and **vertebra** are particularly associated with loss of mobility and risk of death. People who suffer a **vertebral fracture** have an **eightfold** increase in mortality compared to other individuals their age.[2]

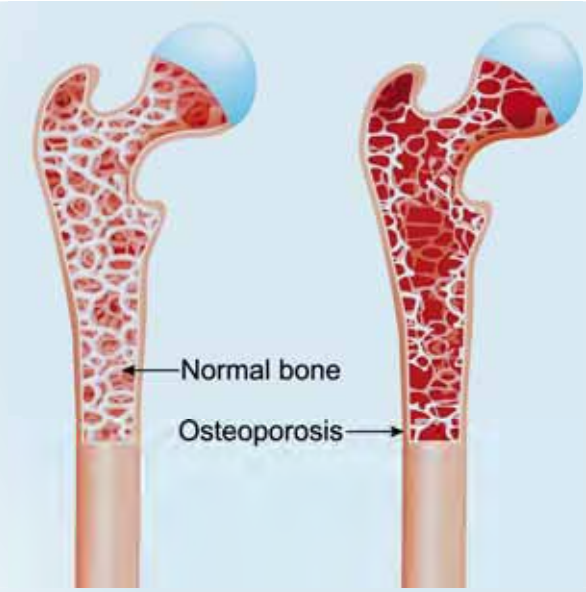
But almost *any* kind of broken bone increases the risk of death in older people.[12] That's why it is imperative to not just slow, but *reverse* bone loss as soon as it begins to take hold.

How Bone Loss Happens

The body constantly breaks down *old* bone and builds up *new* bone.

In the first decades of life, **bone density** increases. Then it plateaus for about two more decades.

At around age 40, bone density begins to *decrease*. In women, the speed of bone loss accelerates with the onset of menopause.



Comparing the left (normal) and right (osteoporosis) images, the increase in dark areas involving this cross-section of the femur are simplified visual depictions of the increase in bone marrow fat, and thinning (decrease) in cancellous/ trabecular bone, that occur with osteoporosis.

This *decline in* bone mineral density leads to a *reduction* in bone strength. Bones become brittle and prone to **fractures**, even from minor injuries and **stress fractures** that occur during normal movement.

Osteopenia is the term for the *early* stage of weakening bones.

If no action is taken and bone density continues to drop, **osteoporosis** develops. Osteoporosis means "***bone full of pores or holes***."

Most people who suffer from osteopenia or osteoporosis are unaware of it until it's too late—when they suffer a **fracture**.

High-Dose Vitamin K2

The good news: There *is* something we can do about age-related bone loss and risk of fractures.

In *low* doses of **45-60 mcg**, vitamin K promotes normal blood clotting. This small amount of vitamin K is normally obtained from dietary sources.

Japanese doctors have long been prescribing much **higher doses** of a specific form of **vitamin K2** as a treatment for **osteoporosis**.[3]

They have amassed decades of evidence that **45 mg** (***45,000* mcg)** of vitamin K2 in the form of **menaquinone-4 (MK-4)**, leads to improvements in bone health.[3]

Now scientists have confirmed that oral intake of high-dose **vitamin K2** is critical for bone strength and other aspects of healthy aging.

Increased Bone Density

Human trials have demonstrated that vitamin K2 maintains or even *increases* bone mineral density. It also helps prevent **fractures**, even in older patients who have already developed **osteoporosis**.[4-11]

In one of these studies, Japanese researchers randomized older osteoporosis patients into two groups. One received **150 mg**/day of **calcium** alone. The other received this same modest **calcium** dose plus **45 mg** of **vitamin K2** (as **MK-4**) daily.[11]

Over a **two-year** period:[11]

- Patients who received *only* calcium continued to lose **bone density**, dropping by about **3%**.
- Patients receiving **vitamin K2** in addition to **calcium** largely maintained their bone mineral density.

A **10%** drop in bone density more than ***doubles*** the risk for **fractures** of the vertebra and hip.[13] This suggests that patients in this study who were treated *only* with calcium may have an increased **risk of fracture**.

But adding **vitamin K2** to calcium largely arrested bone loss, possibly preventing an increase in fracture risk.[11]

Patients receiving K2 also had a significant *increase* in levels of active **osteocalcin**.[11] This protein binds calcium to bone, helping the body turn calcium into healthy ***new bone***.[14]

Preventing Fractures

In the same study, scientists assessed the effect of **vitamin K2** on the incidence of bone **fractures**.

During the two-year study, the group receiving **calcium alone** sustained **35 fractures**, compared to only **14 fractures** in the **vitamin K2** group.[11]

In another Japanese clinical trial, scientists evaluated the effect of vitamin K2 on **women** with **osteoporosis**.[6]

Taking **45 mg** of oral vitamin K2 daily:[6]

- Maintained **mineral density** to a significantly greater degree than in the untreated group, and
- *Reduced* the incidence of vertebral **fractures** to a degree similar to the drug **etidronate**.

Etidronate (most commonly sold as Didronel®) is from the class of drugs known as **bisphosphonates**. It is used to treat **Paget's disease**, a condition characterized by bones that are soft, weak, or easily broken.

It is sometimes used to treat osteoporosis, but its side effects can include nausea, diarrhea, heartburn, chest pain, and skin blisters.[15] Vitamin K2, on the other hand, is not associated with significant side effects.

How Vitamin K2 Keeps Bones Strong

Vitamin K2 works by restoring a healthy balance between the two types of bone cells that influence **bone density**: osteoclasts and osteoblasts.

Osteo*clasts* break down old bone. **Osteo*blasts*** build new bone.

Healthy bone relies on a *balance* of activity between these two types of cells.

WHAT YOU NEED TO KNOW

Better Bone Health with High-Dose Vitamin K2

- **Osteoporosis** causes bone loss and increases the risk of serious **fractures**. In people over 50, these fractures are a significant mortality risk.
- **High-dose vitamin K2,** in the form of **MK-4,** has been used in Japan for decades as a treatment for osteoporosis.
- Human trials have shown that daily intake of **45 mg** of **vitamin K2** (MK-4) maintains or *increases* bone density and cuts the risk of fractures.
- Other vitamins and minerals, including **calcium** and **vitamin D3**, also support bone health, and help maximize vitamin K2's benefits.

Medications That Promote Osteoporosis

Many common drugs can contribute to bone loss and osteoporosis risk, including:

- **Cancer-fighting drugs** that inhibit sex hormones. These include **anti-androgen** therapies (which reduce levels of testosterone) and **aromatase inhibitors** (which reduce estrogen activity).[36,37]
- **Corticosteroids** like prednisone, hydrocortisone, dexamethasone, and many others.[38,39]
- **Warfarin** (Coumadin®), which is used to treat blood clots.[40-42]
- **Proton-pump inhibitors** used to reduce stomach acid, including Nexium®, Prilosec®, and Prevacid®.[43]

No one should stop taking these medications unless directed by their doctor. But people using any of these drugs may want to carefully monitor their bone mineral status.

Aging disrupts this delicate balance. Osteo*clast* activity overtakes osteo*blast* activity. Bone is broken down faster than new bone is built up. Bone **density** drops and **osteopenia** and **osteoporosis** result.

Vitamin K2 has been shown, in preclinical studies, to promote:[14,16]

- An *increase* in bone-building **osteoblast** activity, and
- A *reduction* in bone-destroying **osteoclast** activity.

With this balance restored, *more* bone is built, *less* is destroyed, and **bone mineral density** is maintained or increased.

Additionally, in order to lay down new bone, osteoblasts need the protein **osteocalcin**. Vitamin K2 helps convert osteocalcin into its *active* form.[14,17]

Nutrients That Support Vitamin K2

The bone-rebuilding effects of vitamin K2 are even greater when supported by several other **nutrients**. The following vitamins and minerals support strong, healthy bones:

- **Calcium** is the major mineral that forms the hard matrix of bone. Most studies show that oral calcium decreases the rate at which bone breakdown and mineral loss occur.[18-20]
- **Vitamin D** helps absorb calcium from the gut after a meal and stimulates the production of **osteocalcin**.[17] It also facilitates the transfer of calcium from the blood and other extracellular fluids to the surface of bones, where it makes them stronger and less likely to break.[21] Vitamin D helps the body absorb the bone-strengthening trace elements zinc and manganese as well.[22,23]
- **Magnesium,** like calcium, makes up the mineral matrix of bone and is needed to maintain healthy bone density.[24]
- **Zinc, Manganese, Silicon, and Boron**. These minerals have been shown to be important for optimal bone formation and health. *Low* intake of each of these minerals is associated with bone *loss*, and increased intake improves bone health in animals and in humans.[25-35]

Supported by these nutrients, **vitamin K2** can provide powerful protection against fractures and bone loss.

Summary

Age-related **bone loss** and **osteoporosis** lead to frequent fractures in people over 50.

High-dose vitamin K2 can help. It improves bone health by restoring balance to the process of bone breakdown and formation.

Doctors in Japan have prescribed it to treat osteoporosis for decades.

Human trials demonstrate that a daily intake of **45 mg** of vitamin K2 maintains or increases **bone mineral density** and reduces the risk of **fractures**.

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

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Vitamin K2's Heart Benefits

Vitamin K2 promotes new bone growth in part by increasing **calcification**, the buildup of calcium deposits, in the **bone**.

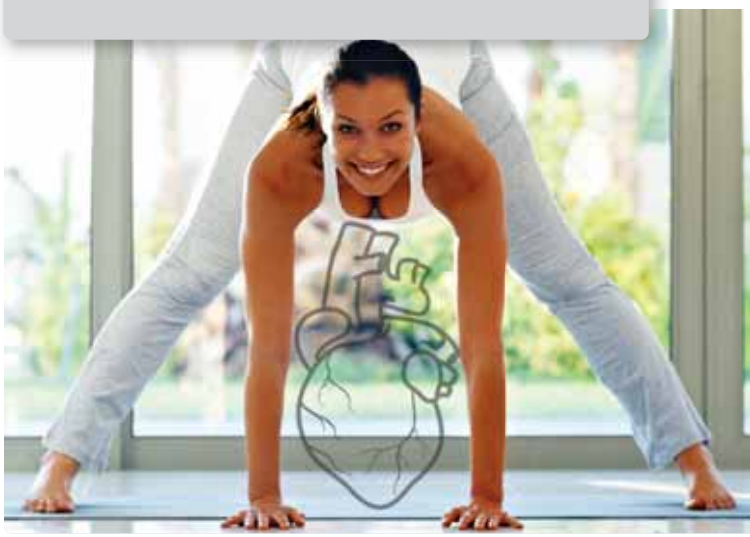
In *soft tissues*, calcification can be dangerous. In blood vessels, for example, it leads to the buildup of atherosclerotic plaque associated with **cardiovascular disease**.

Research has shown that while vitamin K2 *causes* beneficial calcification in bones, it *prevents* harmful calcification in soft tissues, including blood vessels.[44,45] This occurs because it activates **matrix Gla protein**, which *inhibits* calcification of blood vessels.

For this reason, vitamin K2 may be protective against cardiovascular disease.[46]

Anyone taking **warfarin**, a powerful anticoagulant, should consult a physician before deciding to take any form of vitamin K.

Warfarin functions by blocking vitamin K activity in the body. Those taking warfarin are told to restrict vitamin K intake even from healthy vegetables. Newer drugs like Eliquis®, Pradaxa,® and Xarelto® provide anticoagulant effects without the need to restrict vitamin K intake.



Combining Vitamin K2 with Osteoporosis Drugs

Bisphosphonates are a group of drugs prescribed to slow the bone loss of osteoporosis. They include **etidronate** (Didronel®), **alendronate** (Fosamax®), **risedronate** (Actonel®), and others.

Research shows that vitamin K2 does *not* interfere with bisphosphonates and can safely be used at the same time.

Some data suggest that they may have an ***additive*** effect. This means they may protect bone density better together than either one does alone.[47]

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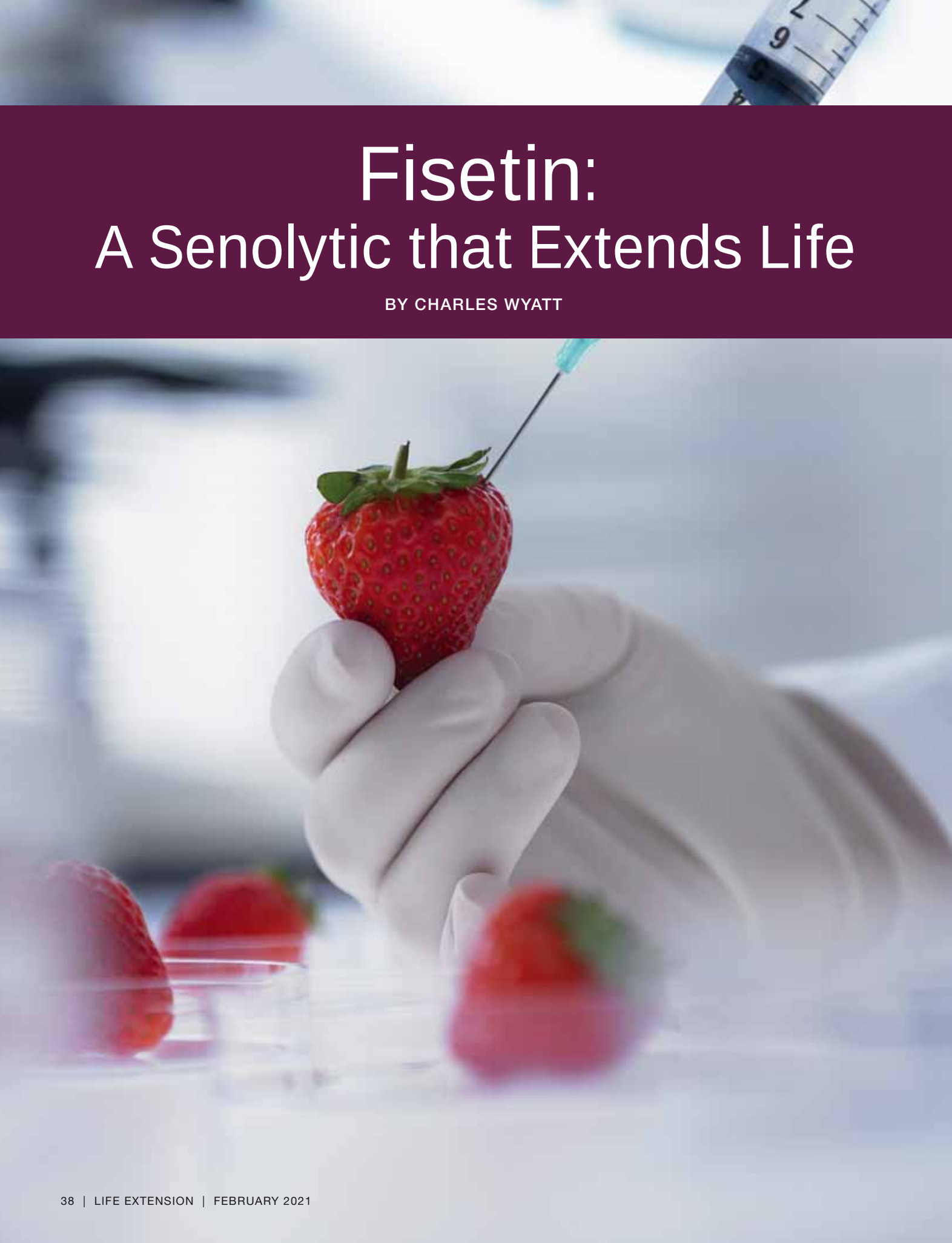
Fisetin:
A Senolytic that Extends Life

BY CHARLES WYATT



Senolytics have been shown to improve health and extend lifespan in experimental models.

These compounds work by helping the body clear away old, damaged (senescent) cells to make way for new, healthy cells.

Fisetin, a flavonoid found in various plants, is ***one of the most powerful natural senolytics*** ever discovered.

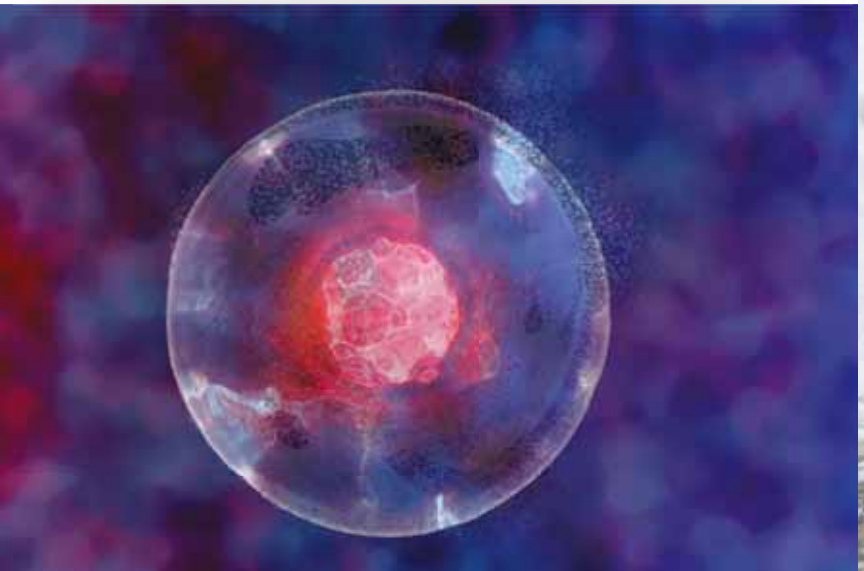
Preclinical and some preliminary clinical studies suggest it may protect against age-related disorders,[1-15] slow certain aging processes, and promote longevity.[10,16]

Old mice given **fisetin** had a nearly **10% increase in lifespan**.[17]

One challenge has been that **fisetin** is rapidly metabolized in the digestive tract. This means very little is ***absorbed*** into the blood stream.

But scientists have developed a way to overcome this problem by combining it with natural compounds from the fenugreek plant.

This novel formulation increased the **bioavailability** of fisetin by as much as **25 times**.[18]



What Is Fisetin?

Fisetin is a flavonoid that has gained popularity in recent years due to its potential health benefits.

It is found in small amounts in many fruits and vegetables, including strawberries, apples, persimmons, grapes, and onions.

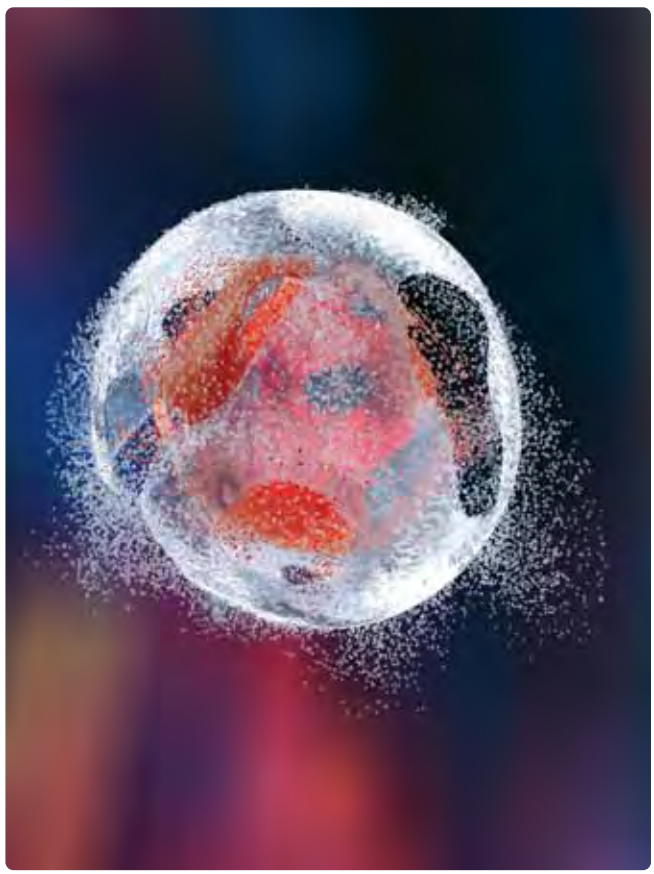
Fisetin shares some of the anti-aging, disease-fighting properties of other polyphenols. Yet it stands out for its remarkable potency as a **senolytic**.[17]

Improved Bioavailability

There's long been a problem with oral fisetin. Soon after ingestion, it is rapidly metabolized in the gut, making it much less effective.

Scientists have now solved this problem by combining **fisetin** with a form of fiber known as **galactomannans**, isolated from the spice **fenugreek**.

This novel formulation has been shown to increase the **bioavailability** (absorption) of fisetin by as much as **25 times**, which may greatly improve its impact on health and longevity.[18]



A Powerful Senolytic

Senescent cells are aged cells that stop functioning properly and can cause damage to surrounding tissues. They lose the ability to grow or divide, and they refuse to die off, earning them the name "**zombie cells**."

These senescent cells spew out compounds that incite harmful systemic **inflammation** inflicting even *more* damage.[19,20]

Senescent cells are a major driver of age-related disease and dysfunction. They even accelerate the aging process itself.

Senolytics are compounds with the ability to *destroy* senescent cells. They hold great promise in the fight against aging and age-related disease, slowing or even *reversing* the aging process.[16,17,21,22]

One of the first senolytics discovered was another polyphenol, **quercetin**, which works effectively when coupled with a chemotherapy drug, **dasatinib**.

Fisetin is a more powerful **senolytic** than quercetin. And it works on its own, without the potential side effects of cancer drugs.

A cell study published in the journal *Aging* showed that it eliminated about **70%** of senescent cells—while doing no harm to healthy, normal human cells.[22]

Another study tested **10** plant-derived compounds, including quercetin, head-to-head. Fisetin was the ***most effective*** at eliminating senescent cells, both in cell cultures and in an animal model.[17]

These findings suggest **fisetin** may be an effective weapon in the fight against aging.

There are a number of **human** trials of fisetin currently in progress.[23] But an animal study has already shown striking results.

When mice that were the human equivalent of **75** years of age were given **fisetin**, they lived an average of 2.5 months longer. That's close to a ***10% increase in lifespan***.[17]

Fighting Oxidative Stress and Inflammation

Fisetin promotes longevity in several other ways.

Oxidative stress and **chronic inflammation** accelerate aging processes and increase risk for chronic diseases.

Fisetin is an **antioxidant** *and* **anti-inflammatory**.

By scavenging harmful free radicals, it *prevents* the damage it does to DNA, proteins, and other cellular components.[24]

It reduces **inflammation** by shutting off pathways that promote it, and by reducing the production of pro-inflammatory compounds.[10]

Mimicking Caloric Restriction

Reducing food intake through a **calorie-restricted diet** has been shown to slow aging, extend lifespan, and improve resistance to disease.[25]

Research has identified the cellular pathways that are affected by such a diet. Among other benefits, caloric restriction:[26]

- Reduces the activity of **mTOR**, a protein linked to aging, weight gain, and chronic disease,
- Boosts the function of **sirtuins**, proteins that regulate cellular health,
- Increases the activity of **AMPK**, an enzyme that regulates metabolism, and
- Promotes **autophagy**, cellular "housekeeping."

Researchers have found that fisetin has a similar effect on ***every one*** of these pathways, mimicking the effects of **caloric restriction**.[10,16,27,28]

For example, **sirtuin** proteins shield cells from damage and help keep them in peak form. But sirtuin function diminishes with age, leading to increased susceptibility to disease and rapid aging.[29,30]

AMPK activity also declines with age, increasing risk for deteriorating metabolic function, obesity, diabetes, and more.[31]

WHAT YOU NEED TO KNOW

The Senolytic Power of Fisetin

- **Fisetin** is a flavonoid found in several fruits and vegetables, including strawberries, apples, grapes, and onions.
- Fisetin is one of the most ***potent senolytics*** yet discovered among plant-derived polyphenols, destroying dysfunctional **senescent cells** and **extending lifespan** by approximately **10%** in animal studies.
- This compound has been shown in preclinical studies to protect against cancer, diabetes, and obesity. In a human trial, it improved outcomes in **stroke** victims.
- Taken orally, fisetin is rapidly metabolized in the digestive tract. Scientists have discovered that combining it with **galactomannans** from fenugreek prevents that from happening.
- A new formulation boosts the bioavailability of oral fisetin by as much as **25 times**, allowing more of it to circulate throughout the body, which may promote longevity and better health.

Several preclinical studies have shown that fisetin *increases* sirtuin function *and* AMPK activity.[32-34] This protects cells and keeps them on a youthful and healthy path.

Protecting the Heart

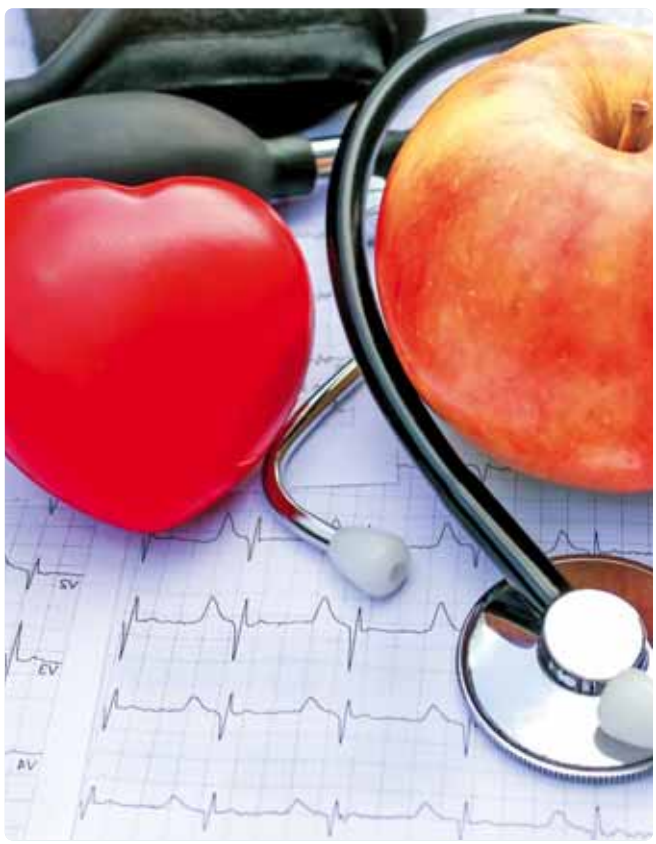
Fisetin not only has the ability to extend lifespan in preclinical models, it may also reduce the risk for many of the most common chronic illnesses.

Heart disease remains the leading cause of death in the U.S. Most common forms of heart disease are due to inadequate flow of blood, oxygen, and nutrients to the heart, which can lead to a **heart attack**.

Over the last two years, studies have demonstrated that fisetin can ***protect the heart*** from injury. Even after **heart attack** models, heart cells fare better when **fisetin** is present.

In one recent study published in the journal *Nature*, rat heart cells starved for nutrients and oxygen were protected by fisetin, preventing cell death.[35]

And in animal models of **heart attack**, the extent of heart damage was *reduced* when treated with fisetin, preserving better heart function.[36,37]



In humans who suffer a heart attack, an **arrhythmia** (abnormal heart rhythm) can often develop.[38] In an animal study, fisetin intake after a heart attack significantly reduced the risk of **atrial fibrillation**, a common arrhythmia that increases the likelihood of stroke or heart failure.[39]

Preventing Obesity and Metabolic Disorders

Fisetin may also help to prevent obesity and common metabolic disorders, like **type II diabetes**.

Obesity predisposes people to higher rates of cardiovascular disease as well as cancer, dementia, and many other conditions.

By *increasing* activity of AMPK and *decreasing* activity of mTOR, fisetin may **reduce weight gain** and protect against related disorders. Even in mice fed a **high-fat** diet, fisetin **prevented weight gain** while protecting the liver, heart, and other organs.[5,10,40,41]

Rodent models of **diabetes** find that fisetin reduces **body weight** and improves **glucose control** and **insulin sensitivity**.[4,12,40-42]

Having better **glucose control** can protect against many of the diabetic complications, like kidney disease, eye disease, and neurological disorders.

Life Extension has long suggested the importance of keeping **fasting blood glucose** between **70-85 mg/dL**, which is challenging for most aging people to accomplish. Fisetin may offer a solution to stubbornly high glucose levels.

Fighting Cancer

As an anti-inflammatory, fisetin may lower the risk of developing cancer.[43-46] But fisetin's **anti-cancer** activity goes even further.

Two recent preclinical studies have shown fisetin to be effective in controlling even some of the most aggressive forms of cancer.

In one, scientists investigated the impact of fisetin on human glioblastoma cells.[47] **Glioblastoma**, a malignant brain tumor, is one of the most invasive and rapidly growing forms of cancer. Even with surgery and chemotherapy, it is usually impossible to control.

Fisetin treatment significantly reduced the growth of glioblastoma cells and even caused them to die off. When directly compared to a chemotherapy drug called **carmustine**, fisetin killed cancer cells at lower doses.

In another recent study, fisetin was effective against several cell lines of **triple negative breast cancer**. This aggressive form of breast cancer is highly resistant to most medical treatments.[48]

In several other studies, fisetin prevented cancer migration and growth while reducing inflammation, enhancing autophagy, and inciting cancer cell death.[11,49-55]

Fisetin may one day be considered as an adjuvant nutritional approach by progressive oncologists.

Brain Benefits

Fisetin has been demonstrated to be **neuroprotective** in animal models of Alzheimer's disease, Parkinson's disease, ALS (amyotrophic lateral sclerosis), and others.[1-3,8-10,15]

In a **2019** clinical study, fisetin was found to help in the treatment of a **stroke**.

Strokes typically occur suddenly, without warning, and can lead to permanent loss of brain function. The most effective medical treatments dissolve or remove the blood clot blocking blood flow to the brain.

But the best chance for success comes when treatment is initiated within **three hours** of the onset of symptoms.[56]

Fisetin has been shown to *extend* this treatment window to **five hours**.[13] While this two-hour extension may not seem huge, it can dramatically increase the number of stroke patients who benefit from clot dissolving and/or clot removing (endovascular thrombectomy) brain-saving therapy.

Summary

Fisetin is a flavonoid found in several fruits and vegetables, such as strawberries and apples.

Recent research has found fisetin to be one of the most effective **senolytic** compounds yet discovered among plant polyphenols. By helping to remove dysfunctional **senescent cells**, fisetin may increase longevity and lower risk for disease.

In mice, fisetin intake **increased lifespan by nearly 10%**, even when started late in life.

Combining **fisetin** with compounds isolated from **fenugreek** allows more fisetin to be *absorbed* and distributed in the body to aging tissues that can benefit from its health-promoting actions. •

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

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Fisetin, a flavonoid found in strawberries and apples, is currently being studied for its effectiveness as a **senolytic** in humans.[1]

In preclinical studies, fisetin:

- Mimics effects of **calorie reduction**[2]
- Targets longevity pathways[2-6]
- Extends lifespan of mice by about **10%**[7]
- Removes **senescent** cells through **senolytic** action[7]
- Suppresses excess **mTOR** activation[8]

Fisetin is poorly *absorbed* due to its breakdown in the small intestines.

Bio-Fisetin solves this problem by enclosing **fisetin** with a compound from the fenugreek herb.

A **human** trial showed **bioavailability** of this new **fisetin** compound increased up to ***25 times*** compared to fisetin by itself.[9]

Just one capsule daily of **Bio-Fisetin** helps manage **senescent cells** and may support overall longevity.

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New England Journal of Medicine Cites Benefits of Intermittent Fasting

BY SUSAN PALMER

Scientists continue to unravel the benefits of **caloric restriction** and **intermittent fasting**.

The simple act of limiting food intake increases lifespan in animal models and reduces age-associated disorders such as diabetes and heart disease.[1-4]

A report published in the ***New England Journal of Medicine*** reviewed extensive research on **intermittent fasting** and caloric restriction. Multiple mechanisms were identified by which these dietary changes are expected to have a beneficial impact on health.[3]

The report found three different **intermittent fasting regimens** to be *just as effective* as true fasting at inducing benefits of **caloric restriction**.

Intermittent fasting, also known as **time-restricted eating**, helps regulate the expression and activity of proteins and other cell factors known to influence health and aging.

Those able to adjust their time of food intake may experience biological changes that boost resistance to disease and help extend lifespan.

Types of Intermittent Fasting

Modern humans have gotten used to eating three meals a day along with frequent snacks.

This constant intake of food has profound adverse effects on our metabolism and health.

Digesting and processing food is a complex, energy intensive process that can accelerate pathological aging processes.

Studies have consistently shown that **intermittent fasting** is superior to constant eating in many ways.

All **intermittent fasting** regimens have regular periods of eating when food and calories are *not* restricted. But their benefit comes from restricting the amount of time that one is eating, and alternating it with relatively long periods of not eating or eating very little.

Three types of intermittent fasting that have been most studied in animal models and human trials and discussed in the *New England Journal of Medicine* are:[3,5]

1. **Alternate-day fasting**. In this regimen, food intake is normal for one day followed by a day of fasting or severe caloric restriction. The pattern is continued indefinitely.
2. **Time-restricted feeding**. In this model, intake of food is restricted to only a small number of hours per day. The rest of the day is spent fasting. One common pattern is to restrict food intake to **six hours** during the day, while fasting the remaining **18 hours**. (Other programs advocate for about 16 hours a day of fasting and an eight-hour eating period.)
3. **5:2 intermittent fasting**. One of the most popular forms of intermittent fasting restricts calories (with a limit of **500-700 calories** per day) on just ***two days*** of each week. Normal food intake is fine on the other five days.

These **intermittent fasting** plans are often easier to adhere to than daily **caloric restriction**.

These three patterns of eating are believed to be equally effective for improving health.

Understanding Fasting

The **fed state** is the period of time when food has recently been consumed.

The **fasting state** occurs after several hours without eating, when nutrients are less available and the body must conserve energy and resources.

Cell metabolism changes dramatically between these two different states.

In the fed state, when nutrients are plentiful, energy is *stored*, often as **fat**.

In the fasting state, as carbohydrates from previous meals are used for energy, fat and other energy-storage compounds are *broken down*.

Some of these fats are converted by the liver into **ketones**, substances that provide an alternative fuel source for the brain and other tissues.

This metabolic shift to ketone metabolism takes time. Ketones in the blood begin to rise **8 to 12 hours** after fasting begins.[3] Most people who eat throughout the day, every day, *never* enter a **fasting** state.

Changes in the Fasting State

When energy availability is low during a **fasting state**, critical changes occur in cellular function.

One of the chief proteins governing cellular processes is known as **mTOR**. During fasting, the activity of mTOR decreases.

Intermittent Fasting from Dawn to Sunset for Four Consecutive Weeks Induces Anticancer Serum Proteome Response and Improves Metabolic Syndrome

- No eating /drinking between dawn and dusk—**14-15 hours** each day
- Average **7.25** pounds of **weight loss**
- Average **8 mmHg** reduction in **blood pressure**
- Significant increase in **tumor suppressor/anticancer proteins**
- Significant decrease in several **tumor promoter/pro-cancer proteins**
- Increase in a protein called **calreticulin** (by around **16 times**)
- Calreticulin enhances **IgG** response to a **SARS-CoV** spike protein

Sci Rep. 2020 Oct 27;10(1):18341.

This leads to an *increase* in **autophagy**, a cellular "housekeeping" process that removes damaged proteins and other cellular debris. Autophagy helps to keep cells functioning optimally.[3]

At the same time, the activities of several other cellular functions are *increased* in a **fasting state** including:[3]

- **AMPK**, which regulates metabolism and energy use,
- **Sirtuins**, which protect against age-related decline and promote longevity, and
- **FOXOs**, which help regulate the expression of genes involved in cell growth, insulin regulation, and longevity.

Increased activity of *each* of the above-mentioned has been tied to longevity and resistance to disease.

Together, they protect cells by repairing DNA, replacing damaged cell parts, producing more mitochondria, and reducing inflammation.[3]

These changes in response to fasting make cells more resilient, healthier, and less prone to disease.

In fact, every one of these functions is being individually investigated by scientists with the goal of extending human life. **Calorie restriction** and **intermittent fasting** positively impact them all.

How Fasting Affects Obesity and Diabetes

Intermittent fasting has been shown to improve metabolism, improving several risk factors for diabetes and heart disease.

Most studies in animals and humans have found that intermittent fasting diets can lead to **weight loss**.[6]

A review of nine studies found that intermittent fasting regimens led to an average **3%** to **8%** reduction in body weight over 3 to 24 weeks.[7]

In one study, subjects lost **2.5%** of their initial weight and **4%** of their fat mass in ***only 22 days***.[8] This is especially remarkable considering that these subjects were *not* obese to begin with.

Intermittent fasting has been demonstrated to *reverse* **insulin resistance** in adults who suffer from prediabetes or full-fledged diabetes.[9,10] In one study, **fasting insulin levels** decreased by **57%**.[8]

Multiple Benefits of Caloric Restriction and Intermittent Fasting

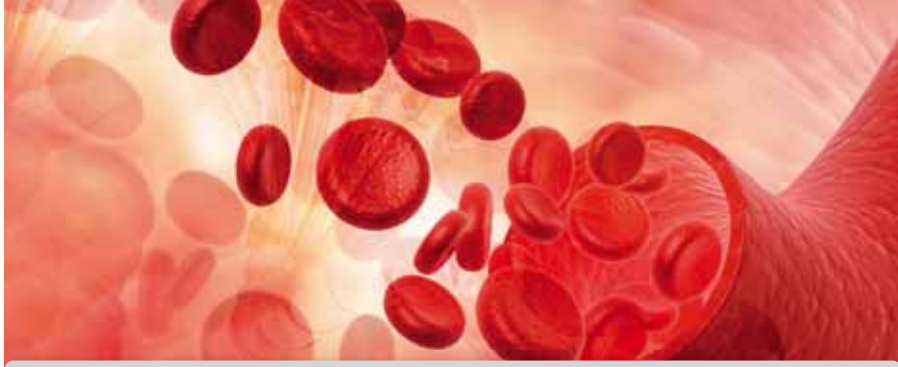
Besides improving insulin sensitivity, caloric restriction and intermittent fasting have been shown to lower blood pressure, heart rate, cholesterol levels, and triglyceride levels.[1,2]

Intermittent fasting also reduces **inflammation**,[11] which is a major contributor to **atherosclerosis**, the buildup of plaque in the arteries.[12,13]

In animal studies, caloric restriction both prevents the formation of tumors and slows the growth of existing **cancers** of various types.[14-16]

Caloric restriction has been found to have cognitive benefits as well, improving verbal memory, working (short-term) memory, higher-level executive function, and overall cognitive function in human trials.[17-19]

In animal models of **Alzheimer's** and **Parkinson's** disease, intermittent fasting has been shown to protect brain cells.[20,21]



A Conflicting Intermittent Fasting Study

The data we are reporting are based on an extensive review article published on **December 26, 2019**, by the ***New England Journal of Medicine***.[3]

This ***New England Journal of Medicine*** article described previous studies showing systemic health improvements in **humans** who restrict food intake to around **six hours** each day. This means they fasted for about **18 hours** on most days.

The authors of this ***New England Journal of Medicine*** article outlined prior studies demonstrating how **intermittent fasting** reduces **abdominal fat** while simultaneously improving most measures of disease risk.[3]

A randomized controlled trial published September 28, 2020, in the ***Journal of the American Medical Association*** (JAMA) was specifically designed to examine the effects of intermittent fasting on weight loss and metabolic risk markers.

The intermittent fasting group in this trial lost a little weight over 12 weeks, while the three-meal/day control group did not lose a statistically significant amount of weight. This study did not find a significant effect on metabolic risk markers.[22]

We've identified reasons why the ***JAMA***-published trial did not find the metabolic benefits reported in a review article just 10 months earlier in the ***New England Journal of Medicine***.

We at **Life Extension®** have long known that **time-restricted eating** (intermittent fasting) does not induce much **weight loss** in those who do not also reduce their overall **calorie intake**.

The preponderance of published evidence, however, continues to support the benefits of **intermittent fasting**. This includes improved **glycemic markers** such as **fasting insulin**. Elevated fasting insulin can impede **weight loss**.[10,23,24]

On **October 27, 2020**, a subsidiary of the scientific journal ***Nature*** reported on a **human** study that only required fasting **14-15 hours** each day.[25] The study group was in poor overall health, with most suffering from nonalcoholic fatty liver disease.

In just four weeks average weight loss was **7.25 pounds**. Even more impressive were significant improvements in cellular proteins that **protect against cancer**.

The box on the previous page summarizes this study showing potential cancer-prevention effects in response to an easier to adhere to fast of **14-15 hours** a day.

In other conditions, notably asthma and multiple sclerosis, clinical evidence suggests that intermittent fasting can help reduce symptoms.[3]

Summary

Caloric restriction and **intermittent fasting** activate proteins and induce metabolic changes that rejuvenate our cells and tissues.

Many studies have shown that these changes prolong life in animals, and reduce risk for many age-related chronic diseases, including cardiovascular disease, cancer, and dementia.

Intermittent fasting is easier for most people to adhere to than traditional fasting and can deliver many of the same benefits. •

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

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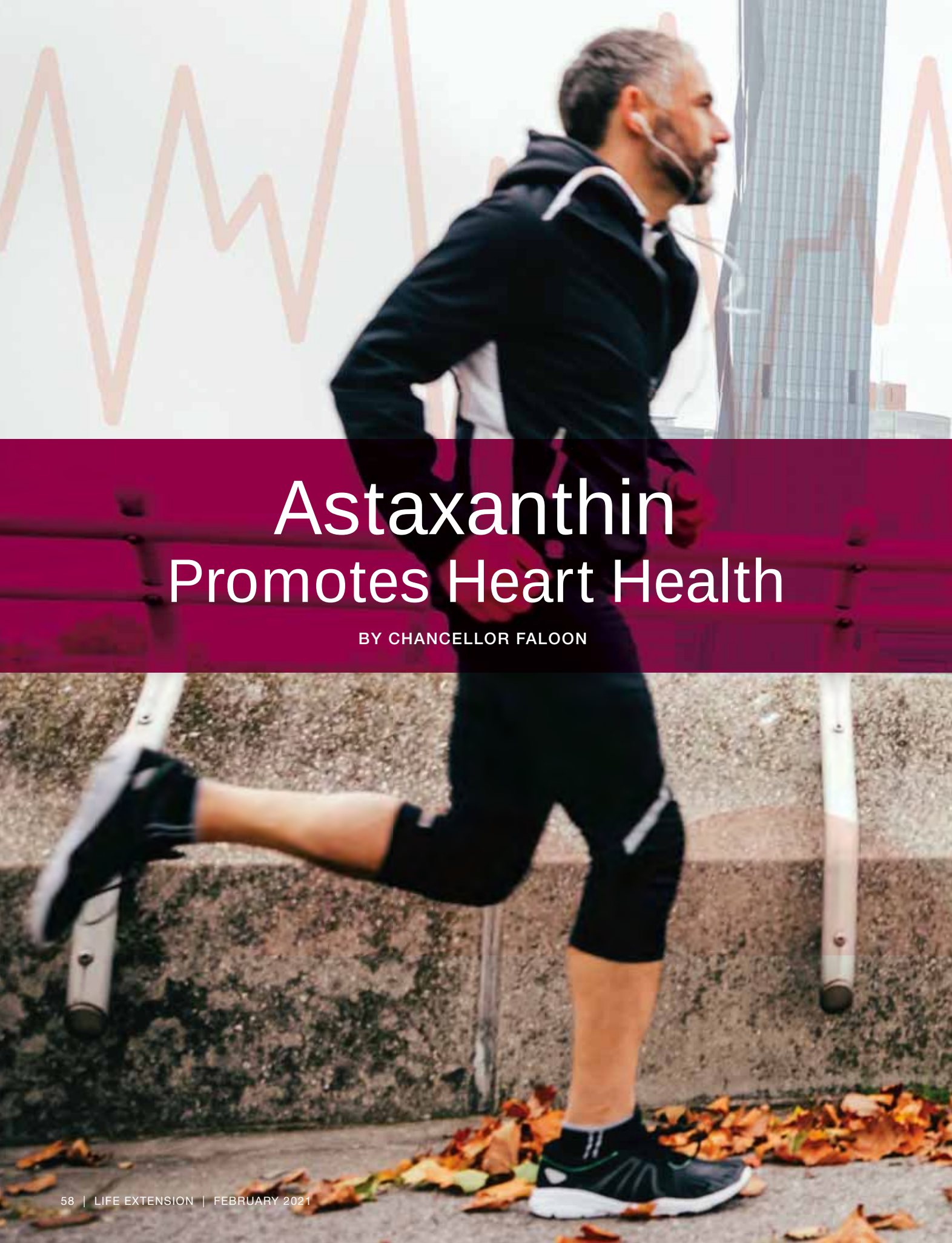


Astaxanthin Promotes Heart Health

BY CHANCELLOR FALOON

Astaxanthin is a **carotenoid** pigment that has long been associated with eye, skin, and brain health.[1-4]

A lesser known benefit is being revealed in studies showing it can also reduce the risk of **heart disease**.

Astaxanthin does this in several ways, including:[5]

- Inhibits **LDL** oxidation,
- Increases **HDL** ("good") cholesterol,
- Supports healthy **glucose** metabolism, and
- Reduces risk of **arterial blockage**.

In one study, mice fed astaxanthin had a **36.5%** *reduction* in the formation of plaque in the **aorta**, the main artery that leaves the heart.[6]

A **2020** prospective pilot study found that three months of **astaxanthin** supplementation *suppressed* **oxidative stress** and *improved* **cardiac contractility** and **exercise tolerance** in **heart failure** patients.[7]

Many people take **astaxanthin** to support overall health. Now there is evidence for an additional benefit: improved **heart health**.

What is Astaxanthin?

Astaxanthin is a red **carotenoid**, a pigment that is especially high in certain microalgae.

It is responsible for the reddish-pink color of flamingos, lobsters, and crawfish, due to the high amounts of astaxanthin they consume.[8]

It is a **free-radical scavenger** and **anti-inflammatory** that provides a wide range of health benefits. Researchers are only now discovering the role it plays in protecting the **heart**.

How Cholesterol Causes Heart Disease

Cholesterol plays a role in the development of **heart disease**.

This waxy, fat-like substance is found in every cell in the body and serves many important functions. Cholesterol provides the raw material for hormone synthesis and provides important components for cell structures.[9-11]

LDL is often referred to as "bad cholesterol." But **small and dense LDL particles** cause much of LDL's harm. The reason is that small and dense LDL particles are more susceptible to oxidation, that makes them more inflammatory and atherogenic.[12]

In **atherosclerosis**, the arteries become clogged and stiff and the flow of blood and oxygen to the heart and brain is reduced. This can eventually result in angina, heart attack, stroke, and **heart failure**.[13]

A Powerful Antioxidant

The molecular structure of carotenoids makes them exceptional **antioxidants**, quenchers of harmful free radicals.

Research has shown that carotenoids can reduce oxidative stress more than certain forms of vitamin E.[18]

HDL (the "good cholesterol") is responsible for *clearing out* excess LDL particles. In a process called **reverse cholesterol transport**, HDL removes potentially dangerous cholesterol particles from the cell and brings them to the liver to be broken down and excreted.[14]

Lab Studies on Astaxanthin

Researchers have discovered that astaxanthin can *increase* **reverse cholesterol transport**.[15]

That may reduce or prevent atherosclerosis, protecting against heart disease and heart attacks.

In one study, researchers tested the effects of astaxanthin on mice genetically bred to have **dyslipidemia** (improper cholesterol balance) and fed a **high-fat diet**.[6]

The mice were divided into three groups:

- High-fat diet plus **astaxanthin**-rich oil
- High-fat diet plus **EPA + DHA**-rich oil
- High-fat diet (control)

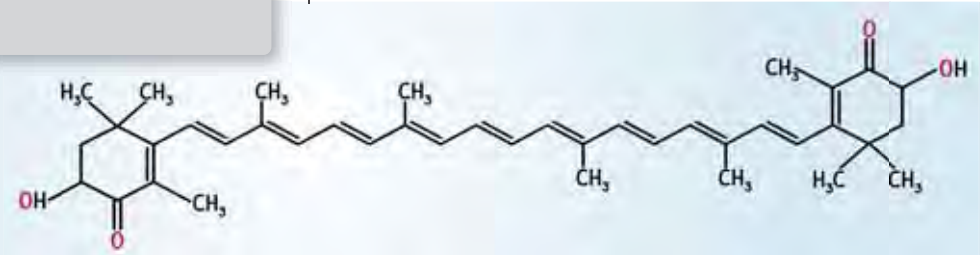
Compared to the control group, both the **astaxanthin** and **EPA + DHA** groups saw reductions in atherosclerotic lesions. In particular, the mice that received the **astaxanthin**-rich oil had:

- A **36.5%** reduction in **aorta atherogenesis** (the development of artery-clogging plaque), and
- A **34.8%** reduction in damage to a vital part of the aorta called the **aortic arch**.

In another study, researchers put rats on a high-cholesterol diet. One group received no treatment and served as a control, a second was given a cholesterol-lowering **statin** drug, a third was given **astaxanthin,** and a fourth group got **lycopene**.

The statin group achieved the greatest benefits. But the groups that received astaxanthin and lycopene also had significantly *reduced* LDL and *increased* HDL compared to the untreated animals.[16]

They also had reduced **foam cells** in the arteries. Foam cells play a central role in the atherosclerotic process.[17]



(**Astaxanthin** – *notice the high amount of conjugated double bonds)*

Heart Benefits in Humans

In 2010, the first randomized controlled **human trial** on astaxanthin was published. It showed that daily supplementation led to a noteworthy *decrease* in levels of harmful **triglycerides** in the body.[19]

Triglycerides are one of the two main types of lipids found in the blood (the other being cholesterol). *High* levels of either increase the risk of heart disease.

In clinical trials conducted since then, astaxanthin has been shown to provide multiple heart health benefits.

Being overweight increases **oxidative stress**, which is closely associated with atherosclerotic disease. In one trial, researchers recruited 23 patients who were overweight or obese and tested whether astaxanthin could *reduce* oxidative stress.[20]

After three weeks of daily astaxanthin intake, markers of oxidative stress *decreased* significantly.

At the same time, levels of **superoxide dismutase** (an enzyme that breaks down the harmful superoxide free radical) and total **antioxidants** (which reduce oxidative stress) *increased* significantly compared to baseline.

The same group of researchers conducted another trial on a different group of overweight or obese patients. This time, markers of **lipids** (fats) were also evaluated, and the trial was extended to 12 weeks.

The results again showed beneficial reductions in oxidative stress. There were also decreased levels of **LDL cholesterol** and **apolipoprotein B** (a marker for LDL particle count), compared to a placebo group.[21]

Controlling Type II Diabetes

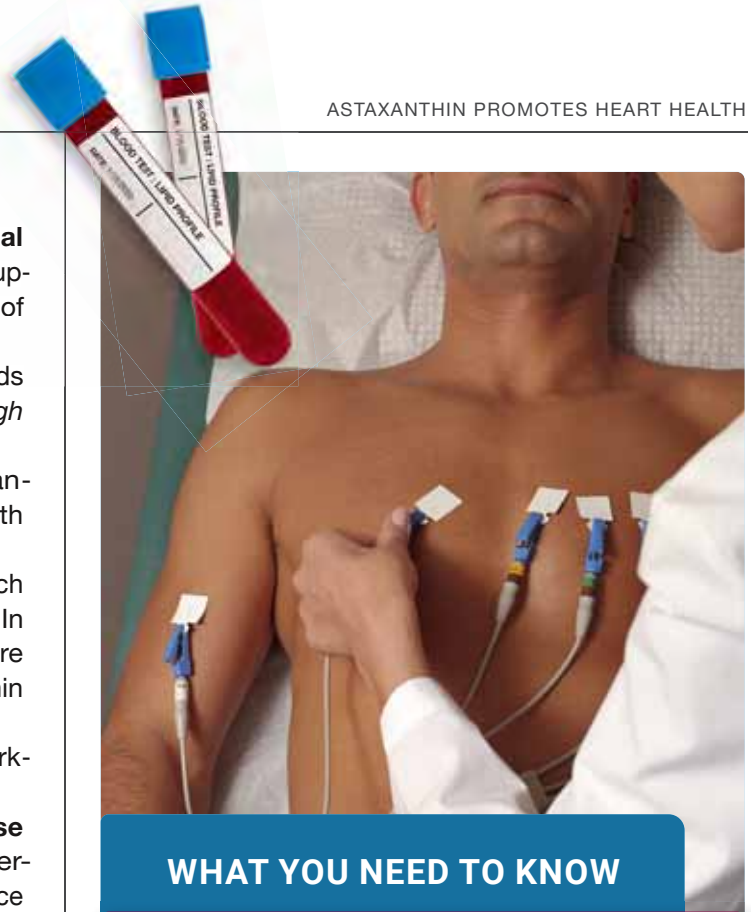
People with **type II diabetes** have a dramatically increased risk of developing cardiovascular disease. Preventing or controlling diabetes protects the heart.

In **type II diabetics**, the body fails to properly metabolize **glucose**, creating an environment in which **insulin** levels are *increased,* contributing to **insulin resistance**.

This **insulin resistance** can be *lowered* by **adiponectin**, a protein hormone that regulates the metabolism of glucose and lipids.[22]

In 2018, a randomized controlled trial of **astaxanthin** was conducted on 44 patients with **type II diabetes**.[23]

After eight weeks, those receiving astaxanthin daily had significantly *increased* adiponectin levels. They also had *reduced* visceral body fat mass, triglycerides, LDL cholesterol, and systolic (the top number) blood pressure.



WHAT YOU NEED TO KNOW

Reduce Risk of Heart Disease

- **Astaxanthin** is a carotenoid pigment with powerful antioxidant and anti-inflammatory properties.
- Recent research has shown that it helps protect the heart and prevent against **heart disease**.
- Among other benefits, it lowers **LDL** ("bad") cholesterol while raising **HDL** ("good") cholesterol, reduces atherosclerosis in animal models, and decreases levels of harmful lipids.
- Astaxanthin also supports healthy glucose metabolism, helping to prevent or control **type II diabetes**.
- The best way to take astaxanthin is in combination with **phospholipids**, which makes it far more **bioavailable** (absorbable).

Most importantly for diabetics, astaxanthin intake *reduced* levels of **glucose** and of **fructosamine**, a compound formed when glucose binds to proteins.

Fructosamine levels are another way to determine glucose averages over a shorter period compared to the **hemoglobin A1C** test.[24]

These actions, together with astaxanthin's cholesterol-lowering effects and other benefits, can help protect against heart disease.

Summary

Astaxanthin is a carotenoid compound that has long been known to provide a wide range of health benefits. Recent research has shown that it protects the **heart** as well.

Studies have demonstrated that it helps reduce dangerous lipid fractions like **apolipoprotein B**, significantly reduce oxidative stress, lower glucose, improve lipid profiles, and more.

These effects may reduce **heart disease** risk and help control **type II diabetes**.

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

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4. **Astaxanthin** for comprehensive eye health support and to fight eye fatigue.[9]
5. **Saffron** to help support vision, based on study subjects seeing an average of two additional lines on eye chart used by doctors to test vision.[1]

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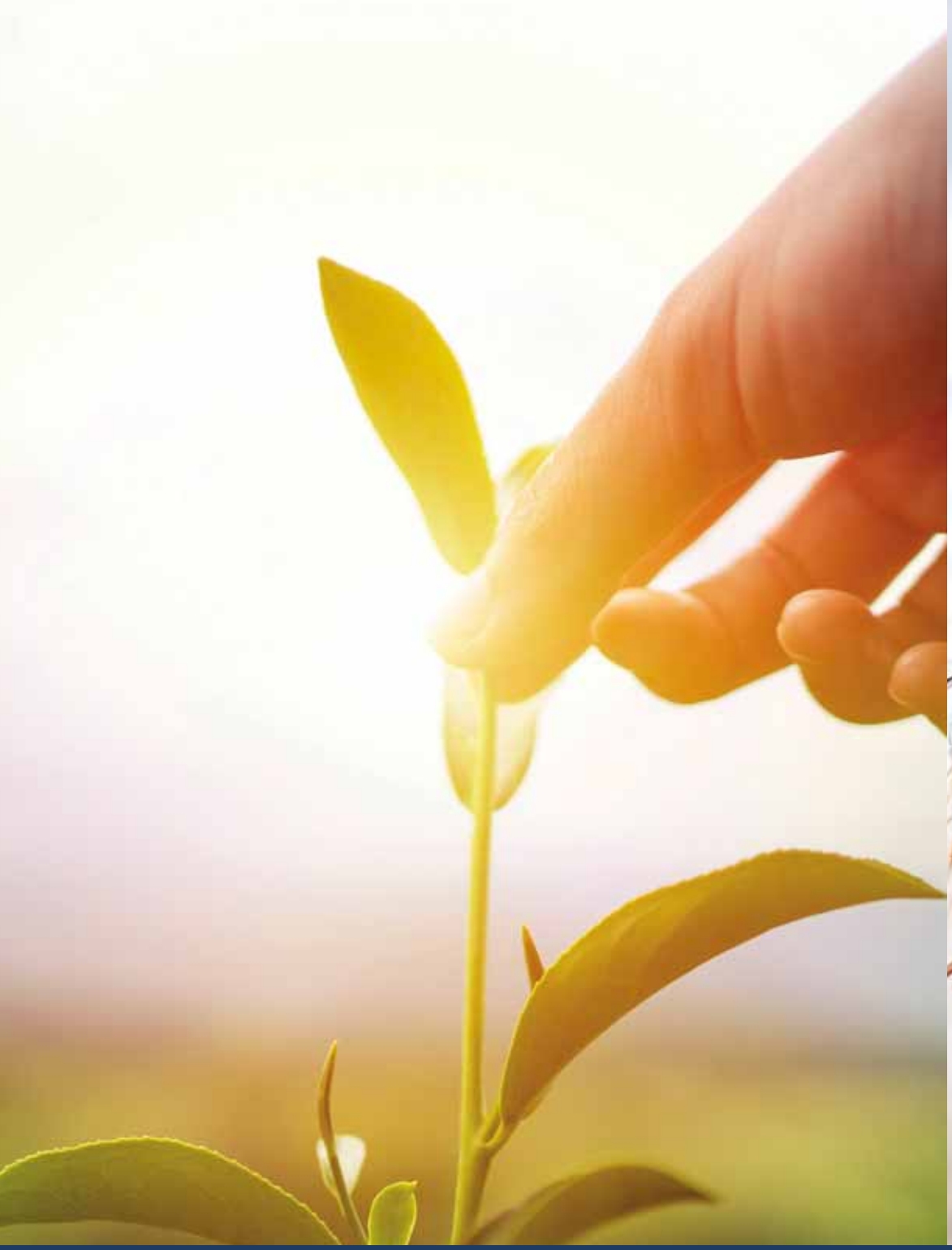

Plant-Derived Compounds that Reduce Chronic Stress

BY STACY KELLER

Doctors are increasingly recognizing the role that **chronic stress** plays in our health and immune systems.

Heart disease, digestive disorders, diabetes, cancer, and most importantly, our immunity can all be impacted by chronic stress.[1-4]

Over the past year Americans have reported feeling an extraordinary amount of stress affecting their well-being.[5]

Reducing the impact of stress has long been recognized as a significant aspect of any wellness program.

Scientists have identified two **plant extracts** that work to reduce stress and anxiety levels.

An amino acid called **theanine**, found in tea leaves, has been shown in clinical trials to relieve chronic stress.[6-8]

Lemon balm, an herb in the mint family, induces calm and **lowers anxiety** levels.[9,10]

Stress Impairs Immunity

In addition to its adverse effect on emotional wellbeing, **chronic stress** may shorten healthy lifespans via several detrimental pathways.[11,12]

Chronic stress ***suppresses the immune system***, impairing the function of infection-fighting immune cells.[2,13]

It also spurs a long-lasting release of the steroid hormone **cortisol** and other signaling molecules that further weaken immune responses.[2]

Chronic stress is associated with increased levels of damaging **inflammation**.[13,14]

Chronic stress is also a factor in many cases of anxiety and depressive disorders.

The World Health Organization has ranked depressive and anxiety disorders as the **first** and **sixth** most important contributors, respectively, to non-fatal negative health outcomes.[15]

There are proven ways to reduce stress, including exercising, eating a healthy diet, and getting adequate sleep.

Scientific research has also identified **nutrients** capable of reducing the stress we feel and the harm that stress does to our body.

Theanine Decreases Stress

Theanine (also known as "L-theanine") is an amino acid primarily found in **green tea**.[6,7,16-18]

Research suggests that its stress-fighting benefits come from its ability to modulate **neurotransmitters** and **hormones** that change how the body responds to **chronic stress**.[19,20]

Theanine *inhibits* the activity of the excitatory neurotransmitter **glutamate**, which rises during stress. It does this by blocking glutamate from binding to receptors in the brain.[17,18]

In a 2019 literature review, researchers present studies showing that a daily dose of theanine, ranging from **200 mg** to **400 mg**, has **anti-stress** and **anti-anxiety** effects that work for both short-term and chronic stress.[16]

Effects on Chronic Stress

In a study of the impact of **theanine** on **chronic stress**, students in an intense pharmacy-practice program took either **200 mg** of theanine twice daily or a placebo, starting one week before the program and lasting 10 days into it.[7]

The subjects were asked how much stress they felt. Measurements were also taken of levels of the enzyme **alpha-amylase** in their saliva. *Higher* levels indicate *increased* levels of stress.[7]

The theanine-treated students had reduced salivary *alpha-amylase* and reported feeling significantly less stress than placebo recipients.

In another chronic-stress study, **200 mg** of theanine daily for four weeks significantly reduced measures of stress and anxiety, while improving sleep quality.[8]

Lemon Balm Promotes Calm

Lemon balm is an herb with a long tradition of medicinal use for alleviating stress, anxiety, and insomnia.[9,21,22]

Lemon balm has been shown to *promote* activity of the neurotransmitter **GABA** (gamma-aminobutyric acid).[10] GABA counteracts the stress-reinforcing effects of **glutamate** in the brain and is associated with a more calm, relaxed state.[23,24]

Studies using **600 mg** of standardized lemon balm extract have shown that it improves mood and lowers perceived stress.[9,10]

WHAT YOU NEED TO KNOW

Lower Stress for Improved Immunity

- Over the past year Americans have reported feeling an extraordinary amount of stress that is affecting their well-being.
- The amino acid **theanine**, found in tea leaves, has been shown in clinical trials to relieve **chronic stress**.
- The herb **lemon balm** also induces calm and lowers **anxiety** levels.
- Controlling the impact that chronic stress has on the body is an essential part of any wellness program.

Summary

A combination of **theanine** and **lemon balm** can ease stress and its damaging effects, without causing drowsiness or loss of alertness.

The amino acid theanine inhibits the action of **glutamate**, an excitatory neurotransmitter that is involved in stress. Excess excitatory stimulation injures neurons.

Lemon balm, an herb in the mint family, complements that activity by increasing the action of **GABA**, a neurotransmitter that *opposes* the stressful effects of glutamate and promotes a feeling of calmness.

These two nutrients can help relieve stress and anxiety and reduce their harmful impact on our body. •

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

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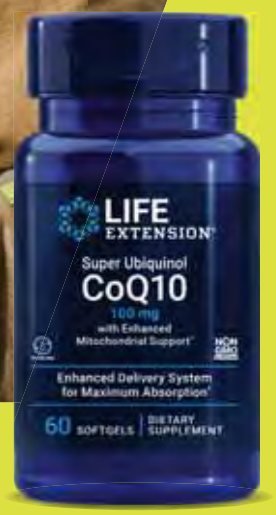

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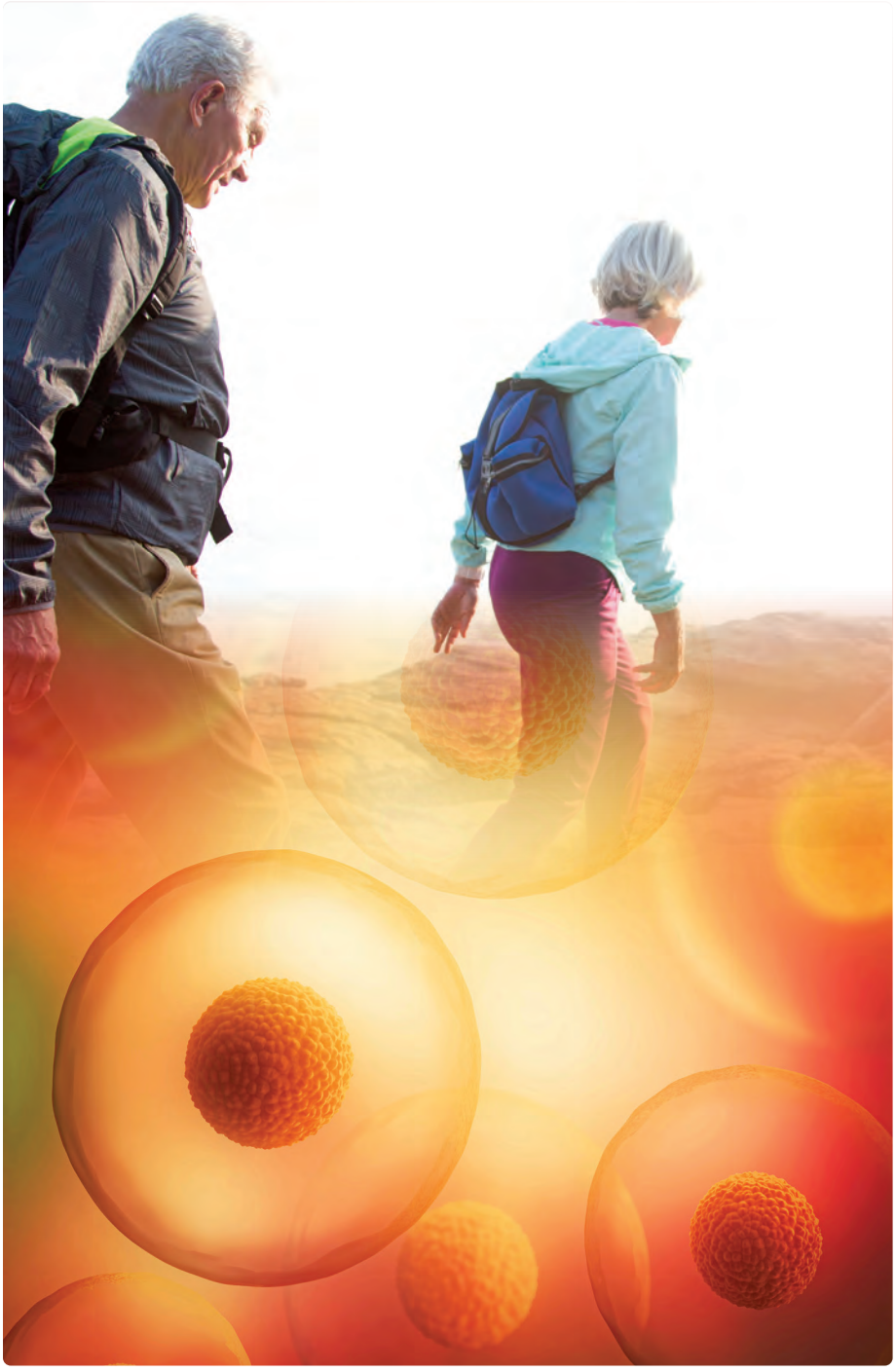
Senolytics for Longer Life

BY DR. ALAN S. GREEN



The medical establishment believes that aging is inevitable and that humans are destined to become old and sick.

Yet, **Dr. Alan S. Green** believes that aging can be managed and delayed through interventions such as senolytic therapies.

In his New York practice, Dr. Green uses **senolytic** compounds to target and remove dysfunctional senescent cells.

These compounds include a drug and two nutrients. By removing old, senescent cells, the body then produces more youthful cells that can slow aging processes and restore more youthful functionality.

In this interview with ***Life Extension***® magazine, Dr. Green discusses the science and theory behind his innovative practice of anti-aging medicine.

LE: You assert that there are two very different types of aging, passive and active. Can you explain your theory?

Dr. Green: ***Passive*** or ***natural aging*** is the classic concept of aging. As a result of wear and tear over time, there is slow accumulation of damage. The damaged parts include mitochondria, DNA, nuclear membranes, proteins, etc. In natural aging, the body does its best to repair the damage which accumulates.

In ***active aging***, the organism's own actions cause damage, decline, and death. This is the type of damage that causes age-related disease. Almost everybody dies from *active* aging.

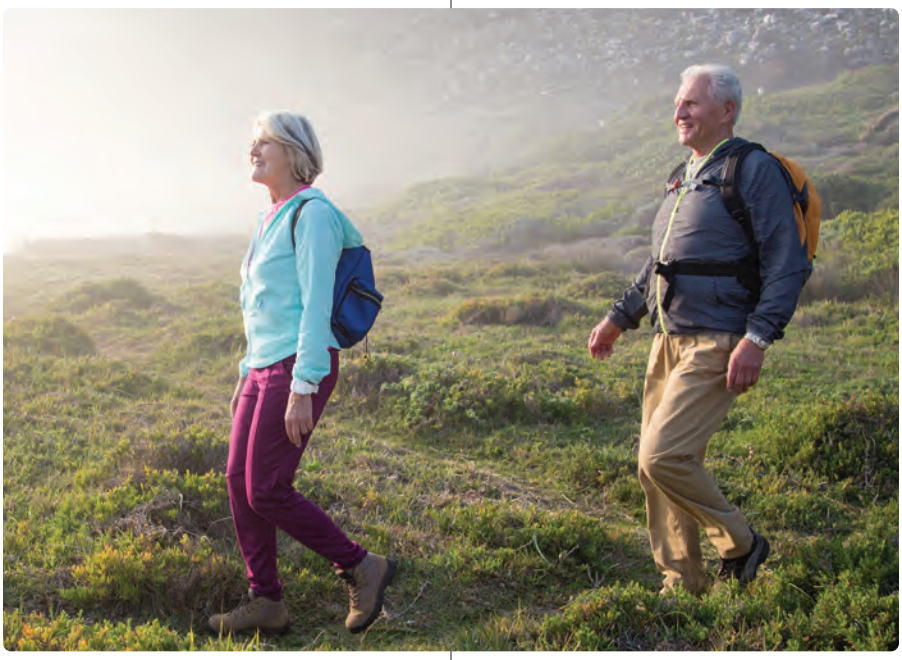
LE: Is it possible to treat or slow active aging?

Dr. Green: Yes. Active aging and age-related disease are driven to a significant degree by two things: **senescent cells** and **mTOR**. They present targets for anti-aging treatments. Drugs or compounds that treat active aging must be able to **prolong lifespan** *and* **prevent age-related diseases**, including atherosclerotic heart disease, Alzheimer's disease, and cancer. In mouse studies, removing senescent cells or lowering mTOR does both of these things.

LE: What exactly are senescent cells?

Dr. Green: Senescent cells have three main characteristics:

1. They are blocked from cell division and can't become two new cells. This has a major impact on tissues that require stem cells to replace lost cells. For example, senescent cells contribute to age-associated **cardiomyopathy** (a disease of the heart muscle that makes it harder for the heart to pump blood to the body). In 70-year-old subjects, over **half** of cardiac stem cells are senescent and can't form healthy new heart cells. This contributes to **cardiac failure**.
2. They cause a damaging bystander effect in neighboring healthy cells, causing *them* to become senescent. In effect, one rotten apple spoils the barrel. In a 2018 study, injection of a small number of senescent cells in young mice spread cellular senescence into host tissues. This led to physical dysfunction and a **five-fold** increased risk of death.
3. They produce what's called a **senescence-associated secretory phenotype**, or **SASP**. This is a witch's brew of highly active substances, including a fearsome mixture of **pro-inflammatory** compounds. Various SASP phenotypes cause specific diseases.



LE: What can we do about senescent cells?

Dr. Green: Senolytics are drugs or other compounds that *remove* senescent cells. In mouse studies, removal of senescent cells increases lifespan and ameliorates age-related disease. There is now a sufficient body of evidence to justify the introduction of senolytics into clinical anti-aging medicine.

LE: What are some effective senolytics?

Dr. Green: The main three senolytics I use are **dasatinib**, **fisetin**, and **quercetin**. Dasatinib is the generic name for Sprycel®, a drug approved since 1996 for the treatment of leukemia. Fisetin and quercetin are flavonoids present in fruits and vegetables. They're sold over the counter and are known to be very safe.

My method is to use all three: **100 mg** dasatinib for three days, **1,000 mg** of regular quercetin for three

days, **1,500 mg** of regular **fisetin** for three days. That's a maximum dose. Patients can begin with a smaller dose and determine sensitivity.

There are now two human studies and more than 20 animal studies regarding dasatinib's role as a senolytic. Quercetin has been used in two human studies, and all mouse studies with dasatinib included quercetin. Fisetin had an excellent result in a 2018 mouse study. It was even *more* effective than quercetin, and there are several human studies using fisetin now listed on: **www.clinicaltrials.gov**. There have been no apparent harmful effects from long-term removal of senescent cells.

LE: What do studies of senolytics show?

Dr. Green: In **mouse studies**, removal of senescent cells improves cardiac function and reduces cardiovascular disease, alleviates frailty and muscle weakness, decreases osteoporosis, improves running endurance, decreases fatty liver disease and lung disease, decreases Alzheimer's-like dementia, and in old mice, **increases lifespan by 36%**.

Two recent **human studies** in **2019** showed that a combination of **100 mg of dasatinib** and **1,000 mg of quercetin**, given orally for three days, removed senescent cells in people with diabetic kidney disease. This showed that senolytics may work similarly in humans as they do in mice.

The other study showed that **100 mg of dasatinib** and **1,250 mg of quercetin**, given for three consecutive days each week for three weeks, alleviated physical dysfunction and improved walking distance and speed in patients with idiopathic pulmonary fibrosis (a lung disease that makes it difficult to breathe). This demonstrated that some of the results in mice can be seen in humans.

LE: What conditions do you think can be treated with senolytics?

Dr. Green: In general, any condition or disease that gets worse with age or has increased incidence with age is likely a senescent-cell-related condition and may respond to treatment with senolytics.

This includes:

- Aging,
- Cancer,
- Cardiovascular disease,
- Alzheimer's disease and neurodegeneration,
- Chronic lung disease and emphysema,
- Chronic kidney disease,
- Non-alcoholic fatty liver disease,
- Obesity and metabolic syndrome,
- Osteoarthritis and osteoporosis,
- Eye cataracts,
- Muscle frailty,
- And more.

LE: Besides senescent cells, you mentioned that the protein **mTOR** plays a role in aging. Can you explain that?

Dr. Green: Since 2009, a large body of scientific studies has shown that increased activity of mTOR (which stands for **mammalian target of rapamycin**, sometimes

called mechanistic target of rapamycin) is a major driver of aging and age-related disease. Many of the harmful actions of mTOR actually relate to senescent cells. mTOR accelerates the production of senescent cells and increases the production of the harmful SASP that senescent cells produce.

LE: How can we reduce mTOR activity?

Dr. Green: It's been shown in some studies that the drug **rapamycin** can increase lifespan in animals by lowering the activity of the mTOR pathway. While senolytics kill senescent cells, rapamycin can help prevent them from developing in the first place. Rapamycin has extended the lifespan of every living thing tested in the laboratory, yeast, worms, flies, and middle-aged mice.

In a 2014 paper, it was reported rapamycin extended the median lifespan **23%** in male mice and **26%** in female mice.

LE: Can you talk a little about rapamycin studies that have been done on humans?

Dr. Green: In a study published in 2014, a **rapalog** (a rapamycin-identical compound) was used to lessen **immunosenescence** (the decline in immune function during aging) in elderly volunteers. It also enhanced response to influenza vaccine by about **20%**. From this study we know that weekly rapamycin may be used to improve immune function in the elderly.

Another study from Taiwan involved the treatment of patients with **acute respiratory distress syndrome** (**ARDS**) due to the H1N1 strain of flu. Patients who were on respirators were given either the influenza drug **Tamiflu®** alone or Tamiflu® with **2 mg** a day of **rapamycin**. Rapamycin reduced the mortality rate from **42%** to **20%** and cut the average number of days patients were on a respirator from **33 days** to **14 days**.

LE: What is your experience with rapamycin?

Dr. Green: Personally, I've been taking **6 mg** of rapamycin **once a week** since 2016. That's an aggressive treatment. A more conservative treatment would be **3 mg** once every **10 days**.

My practice has been treating patients with intermittent rapamycin for over three years. We now have more than **500** patients. Rapamycin is a prescription drug and should be used under a doctor's supervision.

However, as regards prescription drugs, rapamycin is both safe and effective.

LE: What do you consider the strongest indication for rapamycin?

Dr. Green: To prevent or delay onset of Alzheimer's disease in the **20%** of population heterozygous for ApoE4 and for the **3%** of population which is homozygous for ApoE4 and faces an **18-fold** increased risk with onset **20** years sooner.

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

Dr. Alan S. Green is a physician based in Little Neck, New York. He is an expert in the growing field of anti-aging medicine. Dr. Green earned his MD from N.Y. State University College of Medicine, Downstate Medical School in 1967.

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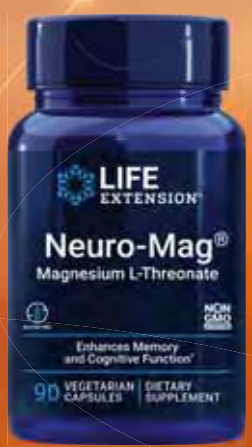

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* *Aging Cell.* 2015 Aug;14(4):644-58.

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Asparagus

BY LAURIE MATHENA

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Asparagus has been consumed in the Mediterranean region for thousands of years. In the sixteenth and seventeenth centuries, it was reserved for use by nobility, and it didn't make its way to the local marketplace until closer to the eighteenth century.

But long before that, the ancient Greeks believed it had aphrodisiac qualities, and it is reported that Hippocrates used it to treat diarrhea.

Now, modern research is showing what makes asparagus so good for you.

Asparagus is one of the most nutritionally well-balanced vegetables, and consuming it may have heart-healthy benefits.

In one study, rats fed a diet with **5%** asparagus for 10 weeks had **17%** lower blood pressure than those fed a standard diet.[1] The researchers found that asparagus contained a compound that in a large enough quantity could work as a natural ACE inhibitor.

Purple asparagus, in particular, contains **anthocyanins**, which are the plant chemicals that give it its distinct purple color.[2] Increased intake of anthocyanins has been associated with:

- Improved blood pressure and lower arterial stiffness,[3]
- Reduced risk of heart attacks,[4] and
- Reduced mortality risk due to cardiovascular disease, coronary heart disease, and all causes.[5]

With a composition of **94%** water,[6] asparagus could be beneficial for weight loss as well.[7]

Asparagus has a distinct flavor that is perfect for grilling in the summertime, roasting in the oven with olive oil in cooler weather, or simply lightly steamed any time of the year.

It also makes a great addition to more complex dishes, like stir fries, frittatas, or salads.

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References

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

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Gordon Ramsay Quick and Delicious: 100 Recipes to Cook in 30 Minutes or Less

Gordon Ramsay is an internationally renowned, multi-Michelin-starred chef who has opened successful restaurants in countries across the world. He is also the star of hit TV shows like *Hell's Kitchen* and *Master Chef*.

But you don't have to travel to France or Singapore or the United Kingdom to indulge in Ramsay's famous fare—and it doesn't take hours in the kitchen to recreate his masterpieces.

In his latest book, *Gordon Ramsay Quick and Delicious*, Ramsay teaches the everyday home cook how to produce some of his favorite mouth-watering meals in 30 minutes or less.

Using bold flavors and aromatic spices, Ramsay proves that quick, simple dishes don't have to compromise on taste or flavor.

While many of the techniques used in the tastiest dishes take time (like marinating, roasting, and slow-cooking), Ramsay gives insider tips that give you all the complexity of flavor in a fraction of the time.

"When I'm home, I don't want to spend hours cooking, but I still want to eat well," said Ramsay. "The recipes in this book are some of my go-to dishes when time is short but the appetite for something delicious is strong."

Before diving into the 100 recipes detailed in the book, Ramsay gives a run-down of time-saving kitchen equipment (good knives, speedy peeler, and stick blender make the list) and adds a few unusual seasoning essentials to have on hand (like harissa and dashi powder).

He also suggests purchasing pre-prepped ingredients, like frozen chopped onions and herbs, spiralized vegetables, and bags of salad greens.

After all, "It isn't cheating to buy pre-prepped ingredients—it's like having a secret sous chef in your pantry and a junior chef in the freezer!" Ramsay said.

Here, ***Life Extension***® highlights three of Ramsay's quick and delicious dishes that are accessible for any home cook.

—Laurie Mathena

Spiced Squash and Lentil Soup

SERVES 4

1 tablespoon light olive oil

3 tablespoons butter

1 onion, peeled and diced

1 teaspoon cumin seeds

4 garlic cloves, peeled

1-inch piece of fresh ginger, peeled

2 red chiles, seeded if you want a milder hit

1 teaspoon mild curry powder

2 pounds butternut squash

1¼ quarts chicken or vegetable stock

1⅓ cups red lentils

1 cup coconut cream

Sea salt and freshly ground black pepper

To garnish

2 tablespoons light olive oil

1 teaspoon cumin seeds

Large handful of fresh curry leaves

½ teaspoon mild curry powder

1 red chile, seeded if you want a milder hit, thinly sliced

1. Heat the oil and butter in a large saucepan over medium heat. When the butter has melted, add the onion and cumin seeds and cook for 2-3 minutes.

2. Meanwhile, place the garlic, ginger, and chiles in a small food processor and blend to a paste. Add this to the pan along with the curry powder and cook for another 2-3 minutes.

3. Prepare the squash by peeling the skin off and removing all the seeds with a spoon. Cut the flesh into 1/2-inch cubes and add to the pan together with the stock. Increase the heat to high and bring to a boil.

4. Add the lentils and cook for 10 minutes.

5. Put the coconut cream into a small bowl and whisk until smooth. Reserve 6 tablespoons for the garnish and add the rest to the pan. Cook over high heat until the squash is soft and the lentils are cooked.

6. While the soup is cooking, heat the oil for the garnish in a small frying pan. When hot, add the cumin seeds, curry leaves, and curry powder. Stir well, then remove the pan from the heat.

7. Using a stick blender, blend the soup until smooth, then season with salt and pepper and ladle into individual bowls. Drizzle over the reserved coconut cream and the curry oil. Sprinkle with a few slices of red chile before serving.

Tuna Steaks with Preserved Lemon Couscous

SERVES 2

2 (7-ounce) tuna steaks

1 tablespoon olive oil

For the preserved lemon couscous

½ cup couscous

Pinch of saffron

½ preserved lemon, finely chopped

½ cup vegetable stock

¼ cucumber

2 tablespoons cilantro leaves

2 tablespoons mint leaves

1 (15-ounce) can of chickpeas, drained and rinsed

2 tablespoons extra virgin olive oil

Lemon juice, to taste

Sea salt and freshly ground black pepper

To serve

½ teaspoon sumac

Lemon wedges

* If you have more time, make the *Moroccan Carrot Salad* to go with this (see next page). It will turn a simple lunch into a feast.

1. Put the couscous into a heatproof bowl. Using a mortar and pestle, grind the saffron to a powder, then place in a small saucepan with the preserved lemon and vegetable stock. Bring to a boil and pour over the couscous. Stir well, cover the bowl with plastic wrap, and leave to sit for 5-10 minutes.

2. Meanwhile, finely dice the cucumber and roughly chop the herbs.

3. Uncover the couscous and fluff it up with a fork. Add the cucumber, herbs, chickpeas, extra virgin olive oil, and a little lemon juice. Mix well and season with salt and pepper. Set aside.

4. Place a large nonstick frying pan over medium-high heat. Drizzle the tuna steaks with the olive oil and season both sides with salt and pepper. When the pan is smoking hot, add the tuna and cook for 2 minutes on each side.

5. Spoon the couscous onto plates and place the tuna on top. Sprinkle each plate with the sumac and serve with lemon wedges and a green salad.

Moroccan Carrot Salad

SERVES 4

1 pound carrots

2 tablespoons rose harissa

1 tablespoon finely chopped preserved lemon

1 green chile, seeded and thinly sliced

2 garlic cloves, peeled and crushed

Juice of 1 lemon

1 teaspoon ground cumin

2 tablespoons olive oil

Large handful of cilantro leaves, roughly chopped

Sea salt and freshly ground black pepper

1. Bring a kettle of water to a boil, then pour it into a saucepan and place over medium heat.

2. Peel the carrots and cut them into thin rounds. Add them to the boiling water, bring to a boil again, then drain immediately. Transfer the carrots to a bowl of iced water to stop them from cooking.

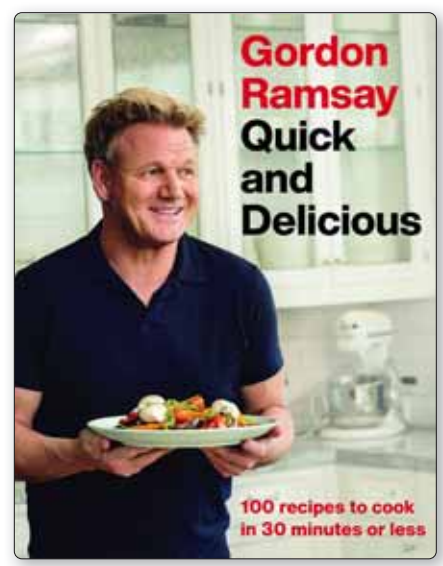
3. Meanwhile, put the harissa, preserved lemon, chile, garlic, lemon juice, cumin, and olive oil into a small saucepan and place it over medium heat for 2-3 minutes to warm through and combine.

4. Drain the carrots thoroughly and transfer them to a serving dish. Spoon over the dressing and stir well. Season with salt and pepper, then sprinkle with the chopped cilantro and stir again before serving.

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

Photo credit: Louise Hagger

To order a copy of Gordon Ramsay Quick and Delicious, call 1-800-544-4440 or visit **www.LifeExtension.com**



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02201 Melatonin IR/XR
01787 Melatonin 6 Hour Timed Release
300 mcg, 100 veg tablets
01788 Melatonin 6 Hour Timed Release
750 mcg, 60 veg tablets
01786 Melatonin 6 Hour Timed Release
3 mg, 60 veg tablets
01721 Optimized Tryptophan Plus
01444 Quiet Sleep
01445 Quiet Sleep Melatonin

VITAMINS

01533 Ascorbyl Palmitate
00920 Benfotiamine with Thiamine
00664 Beta-Carotene
01945 BioActive Complete B-Complex
00102 Biotin
00084 Buffered Vitamin C Powder
02229 Fast-C® and Bio-Quercetin Phytosome
02075 Gamma E Mixed Tocopherol Enhanced with
Sesame Lignans
02070 Gamma E Mixed Tocopherol/Tocotrienols
01913 High Potency Optimized Folate
01674 Inositol Caps Liquid Emulsified
02244 Liquid Vitamin D3 • 2,000 IU, 1 fl oz
02232 Liquid Vitamin D3 • 2,000 IU, 1 fl oz, mint
01936 Low-Dose Vitamin K2
00065 MK-7
00373 No Flush Niacin
01939 Optimized Folate (L-Methylfolate)
01217 Pyridoxal 5'-Phosphate Caps
01400 Super Absorbable Tocotrienols
02334 Super K
02335 Super K Elite
01863 Super Vitamin E
02028 Vitamin B5 (Pantothenic Acid)
01535 Vitamin B6
00361 Vitamin B12 Methylcobalamin
01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges
01537 Vitamin B12 Methylcobalamin • 5 mg, 60 veg lozenges
02228 Vitamin C and Bio-Quercetin Phytosome
1,000 mg, 60 veg tablets
02227 Vitamin C and Bio-Quercetin Phytosome
1,000 mg, 250 veg tablets
01753 Vitamin D3 • 25 mcg (1,000 IU), 90 softgels
01751 Vitamin D3 • 25 mcg (1,000 IU), 250 softgels
01713 Vitamin D3 • 125 mcg (5,000 IU), 60 softgels
01718 Vitamin D3 • 175 mcg (7,000 IU), 60 softgels
01758 Vitamin D3 with Sea-Iodine™
02040 Vitamins D and K with Sea-Iodine™

WEIGHT MANAGEMENT & BODY COMPOSITION

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

WOMEN'S HEALTH

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

HIGHER POTENCY
CARNOSINE

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

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

SUPER SALE PRICE
Item #01829 • 60 vegetarian capsules
1 bottle **$24.30** • 4 bottles $21.60 each

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

SUPER SALE PRICE
Item #02020 • 60 vegetarian capsules
1 bottle **$27** • 4 bottles $24.30 each

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

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

GLUTEN FREE
NON GMO LE CERTIFIED

45 times Greater Bioavailability

Curcumin

Patented **turmeric extract** (500 mg) results in **45 times** greater bio-availability of free curcuminoids.

SUPER SALE PRICE • Item #02407

500 mg, 60 vegetarian capsules

1 bottle **$21.60** • 4 bottles $19.80 each

Same 500 mg potency patented **tumeric extract** with added benefits of ginger and other turmeric actives.

SUPER SALE PRICE • Item #02324

500 mg curcumin + gingerol, 30 softgels

1 bottle **$18** • 4 bottles $16.20 each

GLUTEN FREE

NON GMO LE CERTIFIED

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

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