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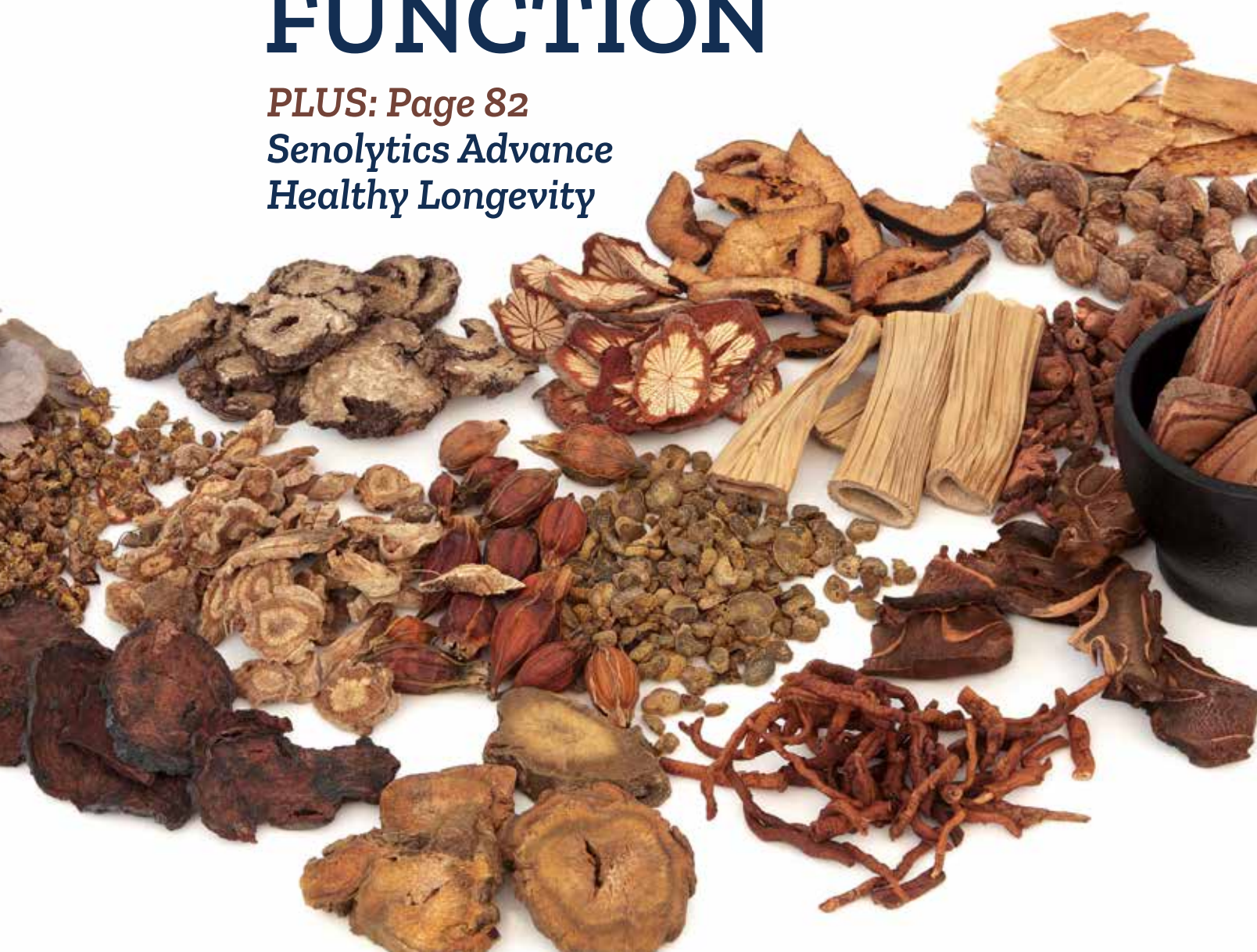
JULY/AUGUST 2021

FEATURE ARTICLES

Impact of Mushrooms on IMMUNE FUNCTION

PLUS: Page 82
Senolytics Advance Healthy Longevity



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CONTENTS

REPORTS

DEPARTMENTS

LIFE EXTENSION®

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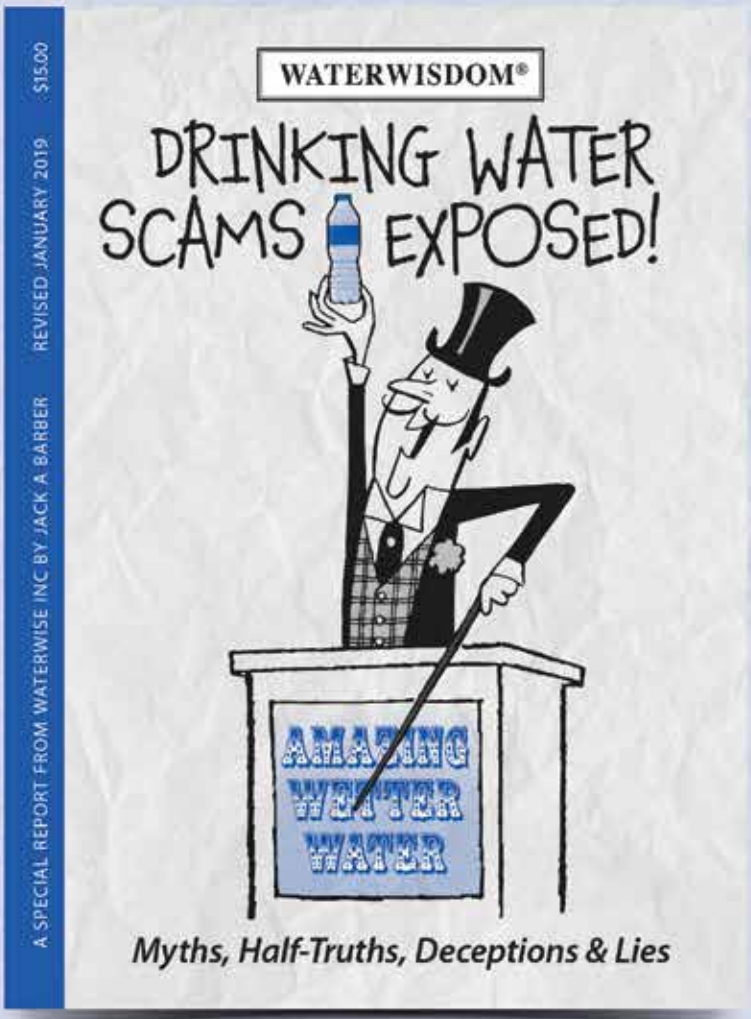

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Aubrey de Grey, PhD, is a biomedical gerontologist and Editor-in-Chief of Rejuvenation Research, the world's highest-impact, peer-reviewed journal focused on intervention in aging. He received his BA and PhD from the University of Cambridge in 1985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

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

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

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In the News

Low Testosterone Linked to Higher Mortality Rate

Men with low levels of **testosterone** have a greater mortality rate from any cause, compared with those who had higher levels, a study published in the *Journal of Clinical Endocrinology & Metabolism* reported.*

The study included 149,436 men between the ages of 40 and 69, who enrolled in the UK Biobank from 2006 to 2010. Blood samples collected at enrollment were analyzed for serum testosterone. The subjects were followed from recruitment through April 2020.

During the follow-up period, 10,053 deaths were documented, including 1,925 from cardiovascular disease and 4,927 from cancer.

Compared to men whose testosterone levels were among the top **20%** of participants, those whose testosterone levels were among the lowest **20%** had a **14%** greater risk of dying from any cause and a **20%** greater risk of dying from cancer during the follow-up period.

Editor's Note: "Serum testosterone concentrations decline with age, while serum sex hormone-binding globulin (SHBG) concentrations increase," the authors stated. They concluded that, "Lower serum testosterone is independently associated with higher all-cause and cancer-related, but not CVD-related, mortality in middle-aged to older men. Lower SHBG is independently associated with lower all-cause, CVD-related, and cancer-related mortality."

* *J Clin Endocrinol Metab.* 2021 Feb;106(2): e625-637.

Healthy Diet Connected to Good Gut Microbes, Lower Disease Risk

In the largest, most detailed study of its kind, researchers found that diets rich in plant-based foods encourage the presence of gut microbes that are connected to a lower risk of diseases like heart disease and type II diabetes, according to an article in *Nature Medicine*.*

Researchers performed deep metagenomic sequencing of 1,203 gut microbiomes from 1,098 people enrolled in the PREDICT 1 study, which included long-term diet information, plus fasting, and same-meal postprandial cardiometabolic blood-marker measurements.

The researchers found significant associations between gut microbes and specific nutrients, foods, and dietary practices. They identified strong microbiome-based markers of obesity, cardiovascular disease, and impaired glucose tolerance.

Editor's Note: People who consumed healthy, plant-based foods were more likely to have high levels of good gut bacteria, while people consuming diets with more processed foods were more likely to have bad gut bacteria, the authors stated.

* *Nat Med.* Feb;27(2):321-332.

CoQ10 Provides Relief from Fatigue

Results from a study published in *Nutrients* reveal a benefit for supplementing with coenzyme Q10 (CoQ10) against mild, daily fatigue.*

The study enrolled men and women aged 20 to 64 who experienced fatigue during their daily lives for at least one month and for no longer than six months.

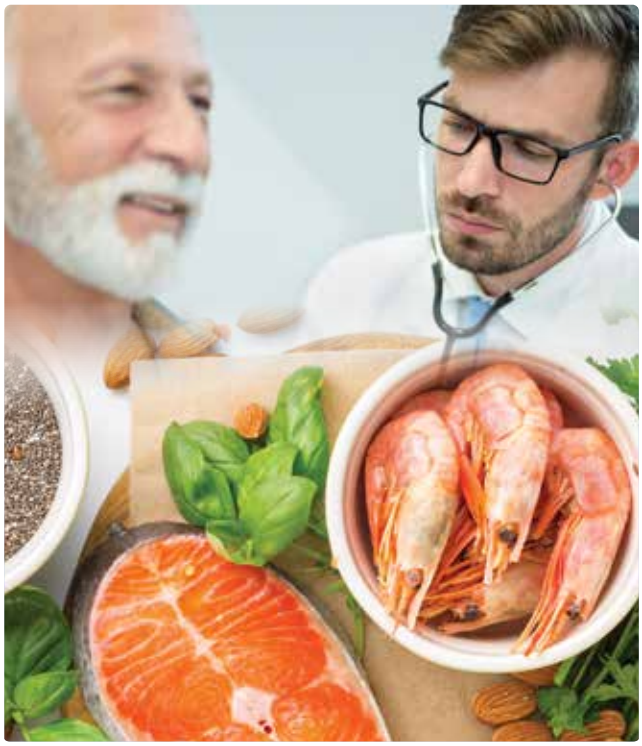
Twenty participants were given **100 mg** of the form of CoQ10 known as ***ubiquinone***, 22 participants received **150 mg** of the ***ubiquinol*** form of CoQ10 and 20 received a **placebo** daily for 12 weeks.

At the end of the study levels of serum ubiquinol, which is the reduced form of CoQ10, were significantly *higher* in the group that received ubiquinol compared to levels measured in those who received a placebo.

Subjective levels of sleepiness or fatigue following cognitive tasks significantly improved in both **CoQ10** groups compared with the placebo group.

Editor's Note: Participants who received ***ubiquinol*** additionally experienced improvement in subjective relaxation following the completion of cognitive tasks, sleepiness before and after tasks, task motivation and serum oxidative stress levels, compared to the placebo group.

* *Nutrients.* 2020 Jun 2;12(6):E1640.



Fewer Adverse Effects After Heart Attack in Those with Greater Omega-3 Intake

An association was found between increased intake of omega-3 fatty acids and a lower risk of clinical adverse effects in patients who experienced a heart attack, the *Journal of the American College of Cardiology* reported.*

The study included 944 patients treated for heart attack with coronary artery stents and/or balloon angioplasty.

Blood samples were analyzed for levels of the omega-3 fatty acids, EPA (obtained from fish), and ALA (alpha linolenic acid), a precursor to EPA/DHA found in plants.

Compared to subjects who had lower levels of EPA at the time of their heart attacks, those who had higher levels had significantly *reduced* risks of experiencing major adverse cardiovascular events and hospital readmission for cardiovascular causes during the three-year follow-up period. Higher levels of ALA were associated with a significantly reduced risk of mortality from all causes during follow-up.

Editor's Note: Consumption of foods rich in these fatty acids might improve the prognosis of heart attack patients, the authors concluded.

* *J Am Coll Cardiol.* 2020 Nov 3;76(18): 2089-2097.

Visceral Fat Decrease Linked with *Higher* Carotenoid Levels

A study reported in *Nutrients* revealed an association between *higher* levels of **carotenoids** and a reduction in visceral **fat** area.*

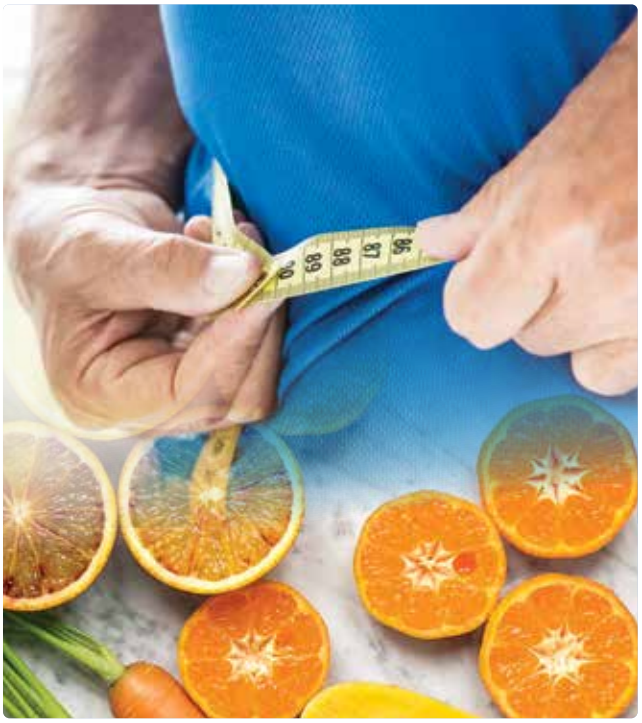
The investigation included 310 men and 495 women who received an annual health examination as part of the Iwaki Health Promotion Project in Japan. Blood samples were analyzed for the carotenoids alpha carotene, beta carotene, beta cryptoxanthin, lycopene, lutein and zeaxanthin. Diet-history questionnaire responses provided information concerning food intake.

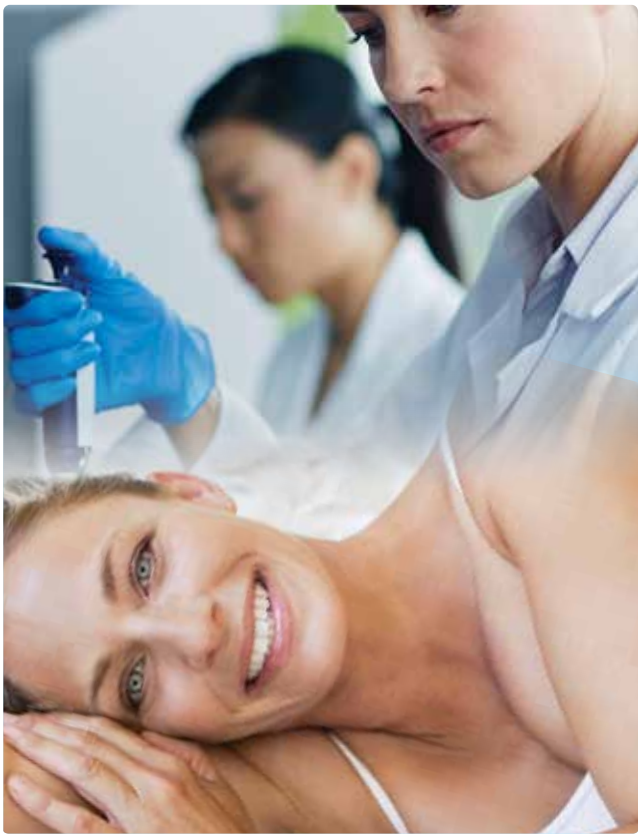
Total carotenoid levels were associated with the intake of leafy green vegetables, carrots and pumpkins, root vegetables and juice. Women's carotenoid levels were significantly higher than those of men.

Higher total carotenoid levels were associated with *decreased* visceral fat area and BMI in women, independent of fiber intake. Increased beta carotene, beta cryptoxanthin and lutein levels in women were also associated with a lower **visceral fat** area.

Editor's Note: "This suggests that consumption of a diet rich in carotenoids (especially lutein and beta-carotene) is associated with lower visceral fat area, which is a good predictor of cardiovascular disease, especially in women," the authors stated.

* *Nutrients.* 2021 Mar 11;13(3):912.





Women's Sexual Well-Being Improves with Testosterone Replacement

Women who receive testosterone hormone replacement have improved sexual function and well-being, according to a review and meta-analysis published in *The Lancet Diabetes & Endocrinology*.*

Researchers studied 46 reports regarding 36 randomized trials with a total of 8,480 female subjects (the majority of whom were postmenopausal). The trials looked at the effects of testosterone on female sexual function, compared to a placebo, or other hormone replacement.

Compared to the control subjects, women who received testosterone experienced improvements in sexual desire, arousal, responsiveness to stimuli, self-image, orgasm, and pleasure, and felt less concern and distress about sex.

Editor's Note: Women can increase their testosterone levels by using prescription **150 mcg** testosterone patches or try **15 mg** a day of DHEA that often boosts testosterone levels in women (but not much in men). DHEA is a low-cost supplement whereas testosterone patches are prescription drugs.

* *Lancet Diabetes Endocrinol*. 2019 Oct;7(10): 754-766.

Gut Microbiome Connected to Alzheimer's Disease

In an animal study, scientists identified a connection between the composition of the gut microbiome and Alzheimer's disease, according to an article published in *Scientific Reports*.*

Researchers compared wild mice with those genetically engineered to carry genes associated with Alzheimer's. They found a connection between gut composition (based on fecal pellets) and behavioral and cognitive performance in these mice.

They also observed a correlation between changes in the gut microbiome and epigenetic regulation of two genes associated with Alzheimer's disease (the apolipoprotein E and Tomm40 genes).

This means the composition of the gut microbiome could play a role in turning on genes that contribute to Alzheimer's disease. Importantly, these changes occurred in the hippocampus, the area of the brain impacted by Alzheimer's.

These findings are consistent with an observational study of people with Alzheimer's disease.

Editor's Note: "The exciting part of this is that you can manipulate the gut microbiome," said senior author Jacob Raber, MD. "We can use probiotics and see what the effect is."

* *Sci Rep* 2021 Feb 25;11(1):4678.

Ashwagandha Root Extract Boosts Cognitive Function

Ashwagandha root extract was shown to improve memory and cognitive function in people with mild cognitive impairment, according to a study published in the *Journal of Dietary Supplements*.*

This double-blind, randomized, placebo-controlled study included 50 adults over age 35 who reported having symptoms of mild cognitive impairment (such as forgetfulness, feeling overwhelmed with decision-making, and drifting thoughts).

The treatment group received **300 mg** of ashwagandha root extract twice daily, and the control group received a placebo.

After eight weeks, the ashwagandha group experienced significantly greater improvements in **general memory** (recall of items such as geometric designs and faces) and **immediate memory** (the ability to recall information over a few seconds, such as a person's name or a telephone number), compared to the placebo group.

The ashwagandha group also experienced greater improvements in executive function, sustained attention, and information processing speed.

Editor's Note: The researchers concluded, "Ashwagandha may be effective in enhancing both immediate and general memory in people with mild cognitive impairment as well as improving executive function, attention, and information processing speed."

* *J Diet Suppl.* 2017 Nov 2;14(6):599-612.

Shiitake Mushrooms Boost Immunity

Eating shiitake mushrooms on a regular basis improves immune function, according to a study published in the *Journal of the American College of Nutrition*.*

For the study, 52 healthy adults between 21 and 41 years old were given a four-week supply of either **5 grams** or **10 grams** of dry shiitake mushrooms.

They cooked the mushrooms at home and consumed a serving every day as instructed.

After **four weeks**, compared to baseline, researchers observed increases in:

- **Gamma delta T cells**, thought to serve as one of the immune system's first lines of defense in epithelial and mucosal tissues,
- **NK-T** (natural killer-T) cells, a type of immune cell which promotes the activity that helps defend against infection, and
- **Secretory IgA** (sIgA) production, which protects the nasal mucosa and respiratory tract mucosal surfaces from infection.

Reductions in **C-reactive protein** (CRP) and *increases* in **anti-inflammatory cytokines** were also seen, suggesting lower **inflammation**.

The researchers concluded that regular consumption of shiitake mushrooms resulted in improved immunity.

Editor's Note: Shiitake mushrooms could also boost heart health, as they contain beta glucans, a type of fiber that can help lower cholesterol.

* *J Am Coll Nutr*. 2015;34(6):478-87.

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

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SUPER K ELITE Item #02335

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Japanese physicians use ***high-dose*** **vitamin K2** for maintaining healthy bone density.

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Prevent Sun Damage from the Inside Out

BY MICHAEL DOWNEY

We all know the one surefire way to help protect against ultraviolet radiation that causes **skin cancer**: use sunscreen.

But a recent study by the U.S. Food and Drug Administration (FDA) reported alarming findings.[1]

At least **six of the most common chemicals** used in most commercial sunscreens—the very chemicals that provide the UV protection—were absorbed into the bloodstream after just one application!

Not only that, but they were found in the bloodstream at levels that ranged from over six times to over ***500 times greater*** than the FDA's recommended safety threshold.

Every single sunscreen chemical tested, in every form of application (lotion and three different types of spray), ended up in the bloodstream in amounts considerably greater than what the FDA considers low risk.

No one should stop using sunscreen. But there are safer ways to protect yourself against the damage UV light can cause.

One option is to use ***sunblock*** containing **titanium dioxide** or **zinc oxide**, mineral compounds that *reflect* UV rays. This is different from the sunscreen chemicals mentioned above that *absorb* UV rays.[2-5]

Another option can be used along with sunblock: an **oral extract** of the fern ***Polypodium leucotomos***. Rather than blocking the sun's rays, it blocks the *damage* they can do.

A randomized controlled clinical trial showed that taking *Polypodium extract* before UV exposure led to a striking ***84% decrease*** in a UV-induced DNA mutation.[6]

For added sun protection, **nicotinamide** enhances DNA repair and reduces UV-induced immune suppression.[7] An **orange extract** from select Sicilian red oranges boosts protection further, reducing sunburn intensity by about **35%**.[8,9]

These nutrients work from the inside out to help protect against sun damage.

Sunscreen Chemicals in the Blood

Skin cancer affects over **three million** Americans each year.[10-13]

Using sunscreen is important. But most topical sunscreens block only a *portion* of harmful ultraviolet radiation from reaching the skin. They also break down over time, reducing their effectiveness.[14]

A new study by the U.S. Food and Drug Administration (FDA) raises another concern. After applying sunscreen to study subjects, and then testing their blood for **six chemicals** used in the sunscreens, scientists found blood levels of those chemicals ranging from over six to over **500 times greater** than the agency's recommended safety threshold.[1]

Both the FDA and the American Academy of Dermatology stress that these chemicals have not been proven to be unsafe. However, they *have* been associated with possible hormone disruption and liver and kidney issues.[15]

Until the health effects of these ingredients are more fully understood, the FDA advises that people continue to use sunscreens.[1,15]

Mineral-Based Sunblock: A Safer Option

Sunscreens come in two types. One contains chemicals and combinations of chemicals that *absorb* ultraviolet radiation. The other contains minerals, such as **zinc oxide** and **titanium dioxide**, that *block* UV rays.[2,4]

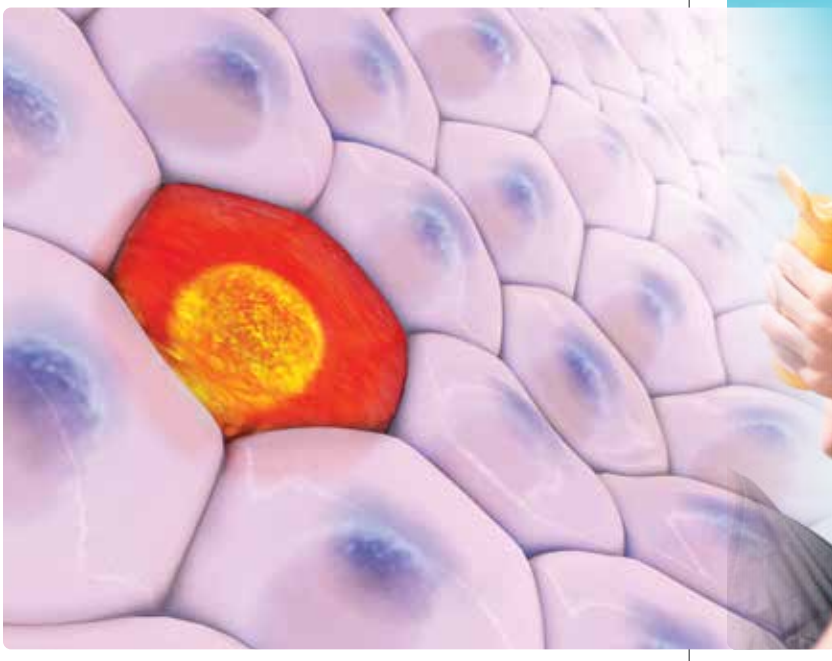
Both the FDA and the Environmental Working Group have determined that **sunblocks** relying on a *mineral* ingredient like titanium dioxide are safe and effective.[2-4] They sit on the skin's surface and act as a shield.

No matter what sunscreen you use, though, it can't provide *total* protection. Among the reasons:[16]

- Sunscreens don't protect the scalp or eyelids,
- Sunscreens may be rubbed off or washed off by perspiration or swimming,
- Most people don't apply nearly enough to block the sun's rays, and
- UV rays penetrate some fabrics in clothes, reaching areas where people have not applied sunscreen.

Scientists have discovered that an extract of a tropical fern called ***Polypodium leucotomos*** offers an ideal addition to topical sunscreens.

It protects the skin against ultraviolet damage caused by the sun. And because it is taken **orally**, it works on all skin areas evenly, and it won't wash or rub off.



How *Polypodium* Works

The sun's ultraviolet radiation causes **premature skin** aging and **skin cancer** by:[17-19]

- Inducing DNA damage,
- Generating inflammation, and
- Increasing oxidative stress.

Research shows that the polyphenols in *Polypodium leucotomos* protect DNA and inhibit oxidative stress as well as inflammation.[6]

Clinically Validated in Humans

Scientists recruited healthy volunteers between ages 29 and 54 and divided them into control and treatment groups.

The treatment group took **240 mg** of ***Polypodium leucotomos*** extract orally, two times, eight and two hours *before* being exposed to UV rays.[6]

Subsequent skin biopsies showed significant *decreases* in DNA damage in the treated subjects.[5]

When subjected to a low dose of UV light,[6]

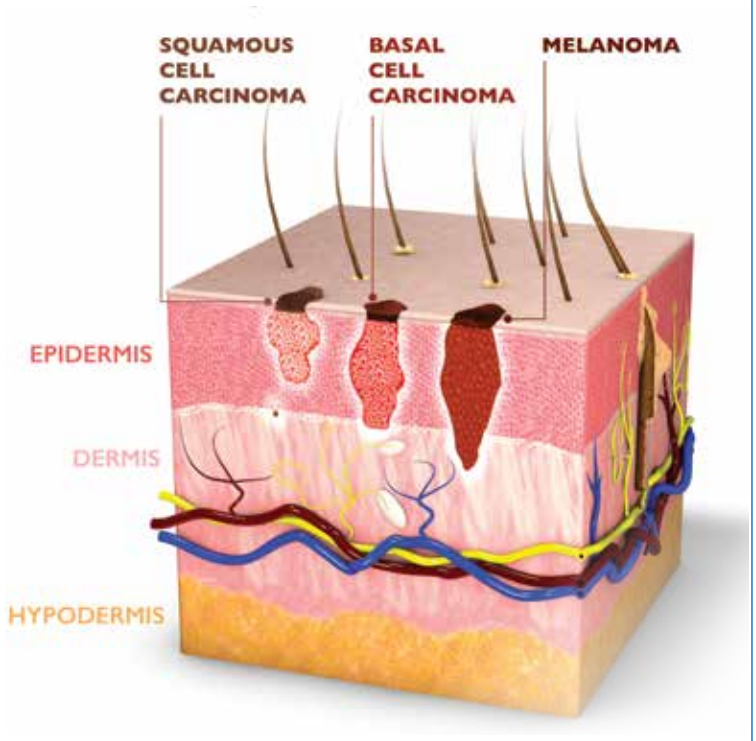
- **Placebo** participants had a **217% increase** in a damaging DNA mutation, while
- ***Polypodium***-taking participants had a striking ***84% decrease*** in that DNA mutation.

WHAT YOU NEED TO KNOW

The Ultimate in Sun Protection

- **Ultraviolet radiation** is a major cause of skin cancer and premature skin aging.
- **Sunscreens** are the first line of defense against UV rays. But a new FDA study found that the chemicals used in most sunscreens are absorbed into the blood at alarmingly high levels after just one application.
- A **sunblock** that contains a *mineral* compound such as **zinc oxide** or **titanium dioxide** is considered safer, but still does not provide complete protection.
- Scientists have shown that a tropical fern extract called ***Polypodium leucotomos*** prevents the UV-induced DNA damage that leads to skin aging and skin cancer.
- Two other nutrients, **nicotinamide** (a form of vitamin B3) and **red orange extract**, further boost sun protection.
- These three ingredients reduce DNA mutations, support the repair of already damaged DNA, lower sunburn intensity and inflammation, and provide powerful protection against skin cancer and skin aging.

TYPES OF SKIN CANCER



When subjected to a *higher* dose of UV light,[6]

- The **DNA mutation** in the **placebo** group increased by a shocking **760%**, while
- The **DNA mutation** in the ***Polypodium*** group increased by only **61%**.

Since DNA mutations are a main cause of prematurely aged skin and skin cancer,[18,20-23] *Polypodium leucotomos* has an enormous potential protective benefit.

Further Sun Defense with Nicotinamide

Two ingredients, **nicotinamide** and **red orange extract**, offer additional protection against sun damage.

Nicotinamide is a form of vitamin B3. Scientists recently completed a review study of its effects, and found that nicotinamide safely:[7]

- Enhances **DNA repair**,
- Reduces UV-induced suppression of **immunity**, and
- Acts as an **anti-inflammatory**.

Ultraviolet radiation normally causes the loss of **ATP** (adenosine triphosphate), the energy-carrying molecule that plays a role in DNA repair.[24] Nicotinamide *prevents* this loss, allowing DNA to be continuously repaired.[25]

In a study that demonstrated this activity, scientists pretreated skin cells with nicotinamide and exposed them to UV radiation. The nicotinamide treatment increased the **removal and replacement of damaged DNA** and significantly increased the number of cells undergoing DNA repair.[26]

A clinical trial further validated that nicotinamide protects against UV-induced **immune suppression**.[27]

These two actions alone—repairing DNA and protecting against immune suppression—powerfully reduce the risk of **skin cancer**.[28]

But **nicotinamide** goes even further. It also:[7,25-30]

- Inhibits production of inflammatory proteins (cytokines), reducing inflammation,
- Regulates skin barrier function, which helps keep moisture in and harmful elements out, and
- Restores cellular energy levels after UV exposure.

Together, these actions can lead to a significant reduction in skin cancers.

In fact, in the randomized, controlled, clinical trials analyzed for the review study, nicotinamide was shown to *reduce* development of new, non-melanoma **skin cancers** in high-risk people.[7]

In one trial, scientists enlisted 386 healthy participants, all of whom had been diagnosed with at least two non-melanoma skin cancers in the previous five years.

This put them into the "**high-risk**" category for future skin cancers.

Twice a day, volunteers received either **500 mg** of **nicotinamide** or a **placebo**. After 12 months, the rate of new, non-melanoma skin cancers in the **nicotinamide** group was reduced by **23%** compared to placebo.[31]

Added Protection from Red Orange Extract

An **extract of Sicilian red oranges** provides an extra layer of protection against UV-induced **inflammation** and **oxidative stress**.

This extract is obtained from pigmented varieties of sweet oranges. Its benefits are due to its abundant **flavonoids** (health-promoting plant pigments) and **hydroxycinnamic acid**, another compound with antioxidant effects.[32-35]

Researchers applied this sweet red orange extract to human **keratinocytes**, the most common type of cell in the epidermis (the outermost layer of the skin). When they exposed these cells to UV radiation, the extract significantly *reduced* inflammation, cell damage, and cell death.[33]

In a human clinical study, oral use of red orange extract **reduced sunburn intensity** by about **35%**.[9] This is extremely significant, because the number of lifetime severe sunburns closely correlates with the development of skin cancers.[36-38]

In another clinical study, volunteers took red orange extract and were exposed regularly to a solar lamp.[8]

After 15 days, the extract had reduced age-spot pigmentation and decreased melanin content from **27%** to **7%**. It also decreased UV-induced sunburn.

The study concluded that **red orange extract** can improve skin appearance and protect the skin against sun damage and **photoaging**, aging of the skin caused by ultraviolet radiation.[8]

Summary

The sun's ultraviolet rays cause DNA damage that accelerates aging of the skin and increases the risk of **skin cancer**.

Studies show that an extract of a fern called ***Polypodium leucotomos*** protects against this UV-induced damage to skin cells and supports DNA repair.

Nicotinamide and **red orange extract** provide additional support for sun protection.

These three nutrients protect skin from the inside out, extending to hard-to-reach areas of the body, and will not rub off.

This potent defense should be combined with a high-quality, high-SPF topical sunscreen, preferably a **sunblock** that includes a safe mineral compound such as **zinc oxide** or **titanium dioxide** to reflect UV rays. •

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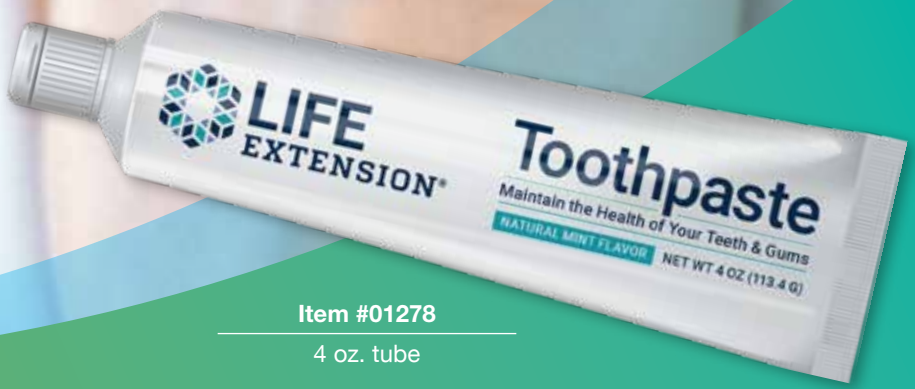

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This product is not a substitute for topical sunscreens.

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

Powerful Defense Against Bloating and Indigestion

BY CHANCELLOR FALOON

After-meal **bloating** is one of the most common and difficult digestive issues.

Up to **30%** of people experience bloating. It tends to come hand-in-hand with other gastrointestinal disorders, such as **dyspepsia** (indigestion), irritable bowel syndrome, and constipation.[1]

Research has identified **four plant compounds** that help relieve bloating and other gastrointestinal problems.

In a clinical trial, **63.1%** of subjects taking an **artichoke-ginger** blend had significantly reduced feelings of bloating, gassiness, nausea, and other symptoms of indigestion.[2]

In another trial, a **fennel-curcumin** combination relieved symptoms of **irritable bowel syndrome**, including bloating and stomach pain, by more than **50%**. This fennel-curcumin blend prevented *all* symptoms in **25.9%** of users.[3]

Taken together, these **four plant compounds** can provide partial or complete relief from digestive miseries.

What Causes Bloating?

Bloating is characterized by trapped gas, abdominal pressure and pain, and a feeling of excessive fullness. It is one of the most frequently reported gastrointestinal issues.[1]

The causes are complex. There can be a wide range of contributing factors, notably including food intolerance, small intestinal bacterial overgrowth, and inflammatory conditions.[1]

But research has revealed that four plant compounds can safely relieve bloating and improve the overall health of your digestive system.

Fennel-Curcumin Relieves Pain and Gas

Fennel and **curcumin** have traditionally been used to aid digestion.

Seeds from fennel, a plant known for its licorice flavor, have long been consumed after meals to promote **digestion** and prevent **flatulence**.[4]

In vitro research shows that fennel reduces gas production by inhibiting the activity of a methane-producing bacterial enzyme.[5]

In addition, clinical trials have shown that fennel seeds, tea, and seed oil stimulate gastrointestinal function, improving gastric motility.[3,6,7]

Fennel also has an antispasmodic effect, reducing irregular muscle contractions that impair normal gut motility.[3]

Researchers combined **fennel seed oil** and a **low-dose curcumin** in a clinical trial to test their effect on bloating and abdominal pain.[3]

Easing Irritable Bowel Syndrome

For the trial, researchers enlisted 121 patients between the age of 18-60 who suffered from **irritable bowel syndrome**. They gave them either a blend of **42 mg** of **curcumin** and **25 mg** of **fennel seed oil** or a placebo, twice daily.[3]

After 30 days, those taking the **fennel-curcumin** blend reported an average **50%** decrease in bloating, abdominal pain, and other irritable bowel syndrome symptoms. This was nearly *double* the **26.1%** decrease in the placebo group.

All symptoms were improved by treatment. Among those taking fennel-curcumin, **25.9%** became ***completely symptom-free***, compared to just **6.8%** of placebo recipients.

The treated group also reported a significant improvement in irritable bowel syndrome-related quality of life, with no adverse effects.

Artichoke-Ginger Mix Aids Digestion

Artichoke influences the production of **bile** from the liver, which helps break down fats, absorb fat-soluble vitamins, and speed up digestion.[8] Italians traditionally serve an artichoke and herbal liqueur after dinner to assist with digestion.

Ginger has been shown in human studies to promote **gastric motility**, the movement of food out of the stomach and into the small intestine.[9,10]

A combination of **20 mg** of **ginger root extract** and **100 mg** of **artichoke leaf extract** led to substantial gastrointestinal improvement in a clinical trial.[2]

The study recruited 126 patients with **functional dyspepsia** (recurring and unexplained indigestion) to receive the combination or a placebo.

Patients rated the severity of six dyspepsia symptoms: fullness, bloating, feeling full after only a small amount of food, nausea, vomiting, and **epigastric** (upper abdominal) pain.

In just two weeks, **44.6%** of participants taking the artichoke-ginger blend had significant improvement in digestive symptoms, compared to **13.1%** of placebo users.

After *four* weeks, **63.1%** of those in the treatment group reported marked reductions in digestive symptoms, compared to only **24.6%** in the placebo group.

Summary

After-meal **bloating**, and other gastrointestinal disturbances can impair our quality of life.

Researchers have identified four plant compounds that target multiple causes of bloating and have shown clinical effectiveness.

In one clinical trial, **63.1%** of subjects taking an **artichoke-ginger** blend experienced significantly reduced gastrointestinal disturbances.

WHAT YOU NEED TO KNOW

Relief for Post-Meal Problems

- **Bloating** is one of the most common gastrointestinal symptoms, marked by a feeling of excessive fullness, gas, and abdominal pressure and pain.
- Scientists have identified **four clinically effective** compounds that target the ***underlying causes*** of bloating.
- A blend of **artichoke leaf** and **ginger root** extracts relieves symptoms of **dyspepsia** (indigestion), including bloating, nausea, vomiting, and upper abdominal pain.
- A mix of **fennel seed oil** and **curcumin** decreases bloating, abdominal pain, and other severe symptoms of **irritable bowel syndrome**.
- Taken together, **ginger root**, **artichoke leaf**, **fennel seed oil**, and **curcumin** may help prevent or significantly reduce gastrointestinal distress and improve quality of life.

In another trial, a combination of **fennel** and **curcumin** was able to completely prevent all gastrointestinal symptoms in **25.9%** of users.

Together, compounds from these four plants may promote a **healthier digestive system** and help protect against bloating, gas, nausea, and other gastrointestinal issues. •

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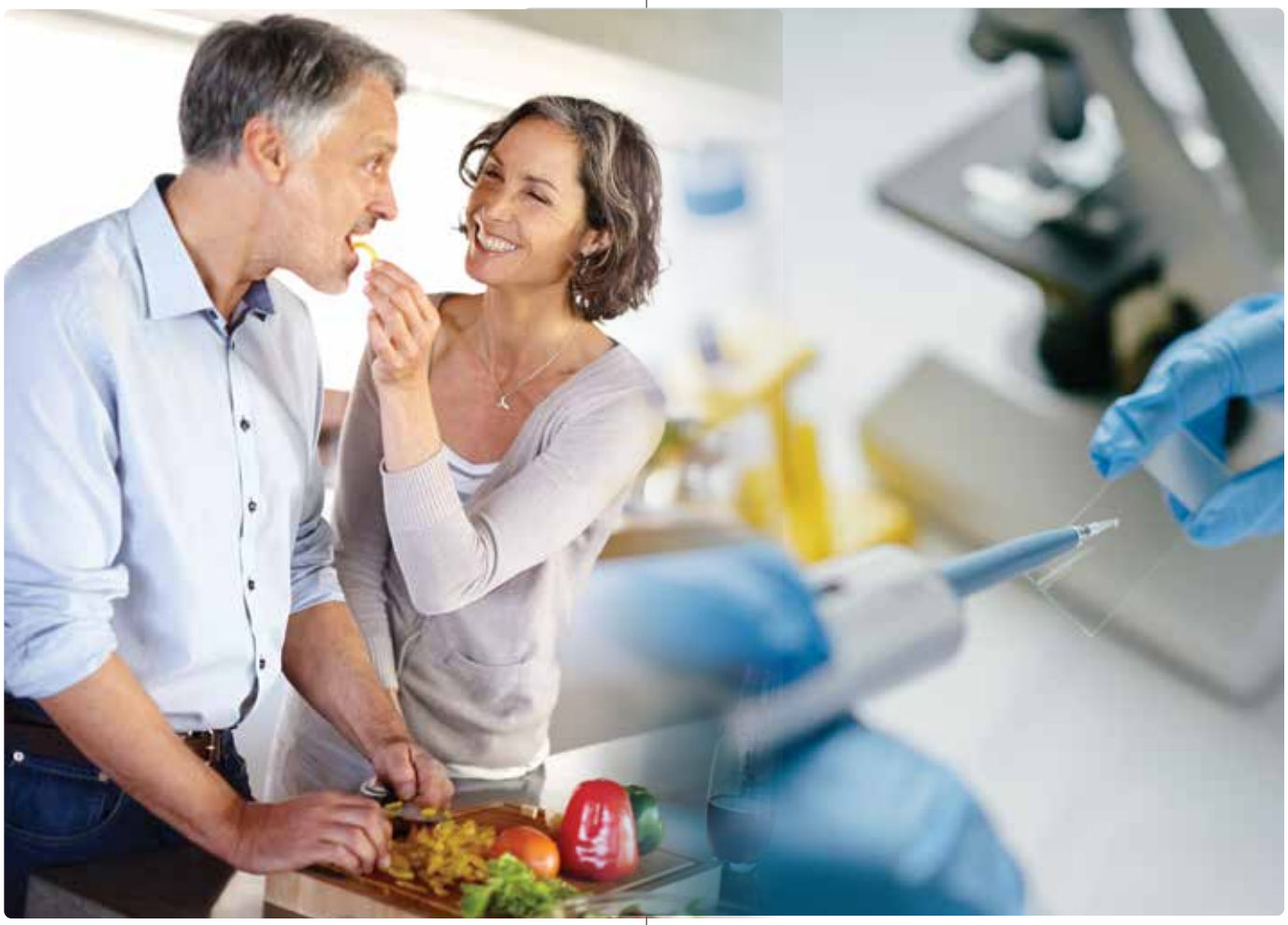

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Immune-Boosting Properties of MEDICINAL MUSHROOMS

BY RONNIE CORTEZ

Mushrooms have been used medicinally around the world for centuries.

They contain compounds called **beta glucans** that are responsible for many of their health benefits, including **antiviral** and **immune-boosting** effects.[1-4]

Studies of **mushroom extracts** *and* isolated **beta glucans** show that these nutrients can help bolster **immune** defenses against infectious diseases.

What Are Beta glucans?

Beta glucans are a group of polysaccharides naturally occurring in cell walls of seaweed, whole grains, fungi, and mushrooms.

Mushrooms, **yeast**, and other **fungi** are particularly rich in **beta glucans** because their cell walls are made up primarily of these compounds.

Beta glucans can help nourish healthy gut bacteria and augment the action of **immune cells** throughout the body.[5]


Chaga

Mushrooms as Medicine

There are thousands of species of **mushrooms**, and many have health benefits.

Three have been found to be particularly effective at supporting **immune health**.

Shiitake

Shiitake mushrooms are a staple of East Asian cuisine and have long been used in traditional Chinese medicine.

In an animal model of severe **bacterial lung infection**, shiitake mushrooms significantly decreased the number of bacteria in the lungs and improved the animals' condition.[6]

Other studies have shown **antiviral** effects against several types of viruses, both by directly inactivating them and by blocking viral replication.[7-9]

Shiitake mushrooms bolster immune defenses by increasing the number of immune system cells, including **T-cells** (which fight specific kinds of viruses) and **natural killer (NK) cells** (which can kill a wide variety of virally infected cells and tumors).[10]

Shiitake also boosts secretion of **antibodies** that protect the digestive tract and reduce **C-reactive protein**, a marker of harmful **chronic inflammation**.[10]

Maitake

Maitake mushrooms grow in various parts of the world and are commonly used in cuisine.

In preclinical studies, maitake was shown to activate immune cells such as **NK cells** and **macrophages** (which are among the *first* immune cells to fight an infection).[11,12]

Extracts of these mushrooms also induce the secretion of **interferons**, proteins that improve the body's ability to defend against infection.[12]

Chaga

Chaga mushrooms grow primarily on birch trees in cold climates, including in northern Europe, Asia, and North America. They are powerful **immunomodulators**.

In a study of mice treated with a drug that *inhibits* **immune system** activity, chaga extract returned levels of immune cells almost back to normal.[13] It also kept down the levels of **tumor necrosis factor**, a marker of potentially harmful inflammation.

This mushroom has been shown in various preclinical studies to have **antiviral** activity against a wide range of viruses. These include various forms of influenza, herpes, hepatitis C, the human immunodeficiency virus (HIV), and others.[14-16]

Natural Immune Support

Mushrooms contain many different compounds. But when it comes to supporting the immune system, **beta glucans** are considered their single most bioactive component.

These polysaccharide compounds can also be isolated from **yeast**.

They work by binding to receptors on an assortment of cells important for **immunity**.[2,3] That activates pathways in the cells that boost their function and help them defend against infection and other threats.

Immune responses can be divided into two types: **innate immunity** and **adaptive immunity**.[17]

1. Innate immunity is the body's first line of defense. It is comprised of sentinel cells that detect and attack a wide range of different viruses and pathogens. Cells of innate immunity include macrophages, neutrophils, NK cells, and others.

2. Adaptive immunity types are the "big guns" that are brought in later to fight off *specific* threats—a particular bacteria or virus, for example—once they have been identified. This also helps the body develop **long-term immunity** to a pathogen. The most important of these cell types are **lymphocytes**, including various B-cells and T-cells.

Beta glucans have a remarkable ability to activate and stimulate *both* **innate** and **adaptive** immunity.[2,3,10,18,19]

They can also help block dangerous inflammation. For example, **endotoxin** is a compound produced by disease-causing bacteria. Endotoxin is often used to induce excess, harmful inflammation in experimental animals. Beta glucans *block* this form of inflammation.[20-22]

A Healthy Gut

A healthy **gut microbiota** (the population of intestinal microorganisms) is also critical to optimal health and fighting **infection**.

In studies, **beta glucans** and **mushrooms** have been shown to encourage the growth of healthy microbiota.[2,23-25] That's because beta glucans serve as **prebiotics**, a source of nutrition for beneficial **bacteria**.[2]

Maitake

WHAT YOU NEED TO KNOW

The Magic of Mushrooms

- Various **mushrooms** have long been used for their medicinal properties.
- These medicinal mushrooms, along with baker's **yeast**, contain compounds called **beta glucans**. These nutrients are responsible for many of the health benefits of mushrooms.
- In studies, mushrooms and beta glucans help strengthen the **immune system** in several different ways, boosting healthy immune responses.
- Along with direct **antiviral** activity, this immune system enhancement helps the body defend against infection and more rapidly eliminate infections that do occur.
- A combination of **beta glucans** from **yeast** along with **shiitake**, **maitake**, and **chaga** mushrooms provides a wide range of compounds to help boost immunity.

These **prebiotics** stimulate the growth and survival of *healthy* bacteria while blocking the growth and development of *disease-causing* bacteria.[2]

As an added bonus, when beneficial bacteria consume beta glucans, they produce **short-chain fatty acids** as a byproduct.[23,25] These compounds support a healthy gut lining, help regulate appetite and metabolism, reduce harmful inflammation, defend against cancer, and more.[26-29]

Countering Immune Senescence

As we age, our **immune system** weakens, a process known as **immunosenescence**.[30]

With the deterioration of immune function, the elderly become more susceptible to infectious disease and cancer.

Studies in animal models of aging have shown that intake of **beta glucans** can help *prevent* or even *reverse* these age-related changes.[18,31]

One study on mice found that by enhancing immune-cell numbers and function, mushroom-derived beta glucans had a **rejuvenating effect** on immune system responses. They had a similar effect on the gut microbiota, reversing negative age-related changes.[31]

Fighting Infectious Disease

The effects of **mushroom** and **beta glucans** have on the immune system can help prevent and treat infection by a range of pathogens.

In animal models, beta-glucan use dramatically ***improves survival rates*** after infection by various bacteria and parasites.[32-35]

Even in cases of infection that are notoriously difficult to eradicate, beta glucans have shown great promise.

For example, in **hepatitis B** infection of the liver, the virus can actively suppress the body's immune response. That leads to chronic infection that can destroy liver function. But in a mouse study, **beta-glucans** isolated from yeast helped the animals to recruit immune cells to the area and clear the virus.[36]

Several human trials of beta glucans have been performed as well.[37-42] Most used a dose of **250 mg** of **beta glucans** isolated from yeast. Subjects were randomized to receive the beta glucans or a placebo.

A number of benefits were observed, particularly in **upper respiratory tract infections** such as the common **cold** and **flu**.

Subjects receiving the **beta glucans** had:

- Fewer symptomatic days,
- Less severe infection symptoms,
- Fewer workdays lost to illness,
- Increased numbers of immune cells in the blood,
- Higher levels of interferon secretion, and
- Increased secretion of antibodies in the saliva, an important defense against digestive tract and respiratory tract infections.

One study looked at a *non*-infectious disorder: **ragweed allergy**. People suffering from this common allergy were randomized to receive either **250 mg** of **beta glucans** or a placebo for four weeks.[43]

Those receiving **beta glucans** had significant *reductions* in total allergy symptoms and symptom severity. Measures of mood, energy, vigor, sleep, and overall quality of life were all improved as well.

This suggests that beta glucans can help improve immune responses not only to infection, but to other forms of inflammation as well.

Summary

Various **mushrooms** have long been used for their medicinal properties.

Compounds contained in their cell walls, called **beta glucans**, are most responsible for these benefits.

Medicinal mushrooms and beta glucans can improve **immune r**esponses, helping to fight various types of **infection** and reduce unwanted **inflammation**.

Beta glucans also help cultivate a healthy **gut microbiota** while resisting the growth of pathogenic bacteria.

A carefully formulated blend of **beta glucans** from yeast as well as **shiitake**, **maitake**, and **chaga mushrooms** can help support healthy immune function. •

Higher Mushroom Consumption is Associated with Lower Cancer Risk

Scientists continue to explore the multiple health benefits of mushrooms.

Researchers at **Penn State University** performed a systemic review and meta-analysis of observational studies published between 1966 and 2020.*

Data from more than **19,500** cancer patients was analyzed specifically for the connection between mushroom consumption and cancer risk. Researchers found that *higher* mushroom intake was associated with *lower* risk of **cancer**.

Further analysis showed that a *higher* intake of **18 grams** per day was associated with a **45%** *lower* risk of **total cancer** compared to an intake of **0 grams** per day.

When site-specific cancer was studied, a significant association was observed with **breast cancer** and mushroom consumption.

Mushrooms, which are low in calories, can be eaten raw as a healthy snack, mixed into a salad, or cooked into different dishes.[44]

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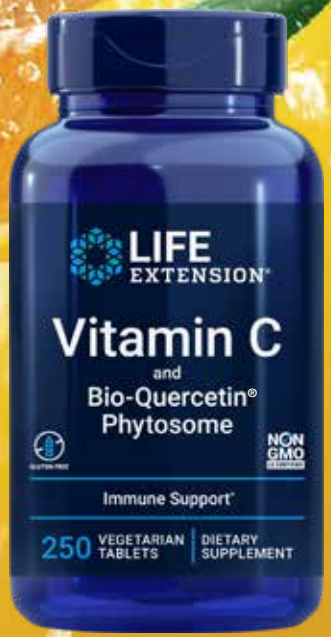

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- Encourage a healthy **gut microbiota**

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BY MICHAEL DOWNEY

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But with age, **ceramide production** *declines*, resulting in dry, sagging skin and wrinkling.[1,2]

Pollution and exposure to ultraviolet (UV) radiation accelerate this skin aging process.[3]

Researchers have found ways to prevent and *reverse* some of this damage with oral ceramides and herbal extracts.

Oral ceramides derived from **rice** are thought to work internally to boost production of ceramides in skin, promoting a more hydrated, youthful appearance.[4,5]

Additionally, researchers have also identified **four herbal extracts** that work together to mitigate skin aging caused by pollution and UV radiation.[6]

In a clinical trial, **96%** of participants taking the herbal extracts had a ***significant reduction in wrinkle depth***.[6]

Taken orally, these nutrients provide a strategic approach to rejuvenate skin and protect against environmental damage.

Ceramides Stop Skin Aging

Ceramides can be thought of like the mortar that holds skin-cell bricks together.

Internal ceramide production declines as we age. This decreases the skin's **moisture barrier**, resulting in thinning, wrinkles, dryness, roughness, and even increased risk of infection.[1,7-12]

Ceramides have been added to some skin creams since the early 1990s. But because ***topically*** applied ceramides do not reach deeper skin layers, their effects are generally modest.[12,13]

To address this problem, scientists developed plant-derived ceramides—or **phytoceramides**—that can be taken **orally**. These lipids are thought to boost the production of ceramides in the skin.

Researchers have now achieved clinical success by using ceramides from a non-genetically modified rice extract that is **gluten**- and ***allergen-free***.[4,5]

Taken orally, these **rice-derived phytoceramides** work from the inside out to hydrate, smooth, and rejuvenate skin all over the body.[4,5]

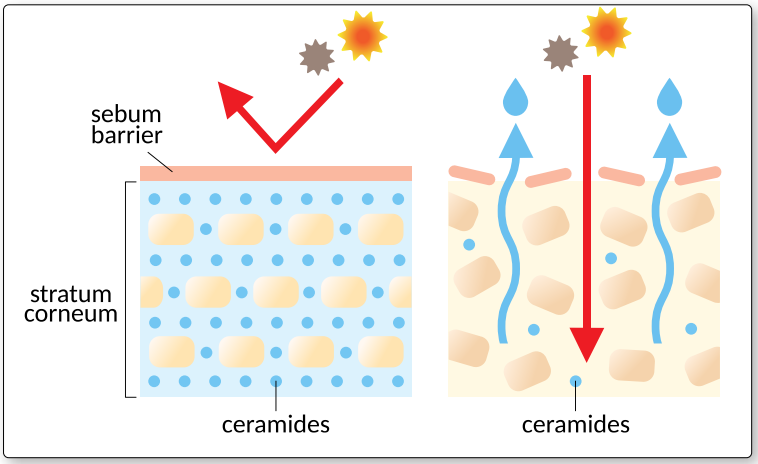
Herbal Extracts Defend Against External Dangers

Age isn't the only factor driving skin damage.

External factors like environmental **pollutants** and **UV radiation** from the sun can degrade the skin's structural integrity, reducing skin firmness and elasticity. That leads to wrinkling and fine lines.[3,14]

In addition to inducing oxidative stress and inflammation, pollutants cause *overexpression* of the protein **aryl hydrocarbon receptor** (AhR).

AhR overactivation increases the expression of genes responsible for oxidative stress, inflammation, immunosuppression, pigmentation, skin cancer, and **premature skin aging**.[6,14]



Researchers have identified four **herbal extracts** that, when taken orally, protect against the damaging effects of pollution and UV exposure as follows:[6]

- Rosemary,
- Olive leaf,
- *Lippia citriodora* (lemon verbena) leaf, and
- *Sophora japonica* (Japanese pagoda tree) leaf.

These extracts have been shown in a **clinical study** to improve skin health and deliver substantial protection against pollutants and UV radiation.[6]

In vitro studies show that the extracts inhibit the overactivation of the **AhR receptor** that causes **premature skin aging** and other skin-damaging effects.[6]

The abilities of rice ceramides *and* this herbal blend to block and even reverse skin aging has been validated in human trials.

Improve Skin Hydration and Barrier Function

Scientists set out to test the effect of **rice-derived ceramides** on **skin barrier function**, the ability to retain moisture and protect against external threats.[4]

They enlisted 123 healthy volunteers with **dry skin**. Every day for 12 weeks, subjects took either **rice extract** providing **ceramides** or a placebo.

Investigators measured water loss that occurs when water passes from the skin's middle layer to the outer layer and evaporates. This test is used as a measure of the skin's barrier function.

In as few as four weeks, subjects taking the rice extract had significant ***reduction in water loss*** through the skin in nearly *all* body areas, compared to those taking a placebo.[4]

A second clinical trial was conducted on patients (mean age: 30.5 years) with **mild atopic dermatitis**, or **eczema**. This skin disease is characterized by impaired skin barrier function and a reduction in ceramide content, and leads to patches of itchy, dry skin.[5]

Every day for four weeks, the treatment group took a **rice extract** providing **ceramides**.

The **placebo group** had significant water loss over the course of the study, resulting in decreased water content in the outer layer of the skin.[5]

Those supplementing with the rice extract ***reduced*** their ***water loss*** by more than **30%** compared to the placebo group. This was seen in visual improvements to skin appearance.[5]

Reducing Wrinkles

Researchers next tested the effectiveness of the blend of **herbal extracts** in guarding against environmental pollutants.

The combination consisted of:[6]

- Rosemary extract,
- Olive extract,
- *Lippia citriodora* extract, and
- *Sophora japonica* extract.

The researchers enlisted 100 women (aged 35-65 years), ***half*** of whom had sensitive skin.

The treatment group took **250 mg** of the blend orally for 12 weeks. The researchers measured an exhaustive list of factors, such as skin moisture, radiance, and smoothness to evaluate the overall look and health of skin.[6]

More than 90% of treated volunteers had significant improvement in ***all*** of the measures.[6]

The **herbal blend** smoothed and softened skin, significantly reduced wrinkle depth, and improved skin elasticity and firmness—beginning in ***just 15 days***.[6]

Compared to a placebo, after 12 weeks of treatment, the group taking the herbal extracts had:[6]

- A **10-fold** greater decrease in **wrinkle depth**,
- A **3-fold** improvement in skin **moisture**,
- **5 times** the skin brightness or **radiance**,
- **2.5 times** more lightening of **dark spots**,
- A nearly **5-fold** reduction in **water loss**, and
- An **18-fold** greater increase in skin **smoothness**.

These improvements in skin appearance are likely due to the reduction in **water loss**, which indicates a clear improvement in the **skin barrier function**.

A strengthened **barrier function** means pollutants are less able to penetrate to the deeper layers of the skin to cause damage.

WHAT YOU NEED TO KNOW

Keep Skin Healthy and Strong

- **Ceramides** are natural oils that keep our skin hydrated and healthy. As we age, our bodies produce fewer ceramides, leading to wrinkles, dryness, and other signs of **skin aging**.
- Scientists have developed **rice-derived ceramides**. Taken *orally*, they have been shown to restore the skin's vital barrier function and youthful skin hydration.
- External factors like environmental **pollutants** and exposure to **UV radiation** also accelerate skin aging.
- A blend of **four herbal extracts** (from rosemary, olive leaf, lemon verbena leaf, and Japanese pagoda tree leaf) defends the skin against the damaging effects of pollution and UV exposure.
- **Vitamin C** provides multiple benefits to skin health, such as promoting collagen formation and reducing dark-spot appearance.
- These ingredients support a healthy, hydrated, and more youthful-looking skin.

Lab studies show that this blend *completely* inhibits the pollution-induced increase in the expression of the **AhR receptor**, which can cause pigmented spots, inflammation, and oxidative stress.[6,14]

Vitamin C Offers Added Support

Vitamin C offers additional benefits for skin health. In studies, **vitamin C** has been shown to:[15-17]

- Promote formation of **collagen**, the skin's main structural protein,
- Reduce **DNA** damage in the skin,
- Scavenge harmful **free radicals**, including oxidants from UV radiation,
- Improve skin **antioxidant** activity *in just two weeks*, and
- Inhibit **melanin** production, reducing the appearance of dark spots.

Most readers of this publication supplement with vitamin C based on compelling scientific findings of its ability to help maintain more youthful collagen levels.

Summary

Skin aging is caused by a variety of factors.

The age-related *decrease* in production of skin **ceramides**, combined with the damaging effects of **pollutants** and **UV radiation**, leads to wrinkles, dryness, and age spots.

Taken orally, **rice-derived ceramides** have been clinically shown to enhance the skin's **barrier function** and boost overall skin hydration.

A blend of **four herbal extracts** protects against the destructive effects of pollution and UV exposure, improving the health and appearance of the skin.

Vitamin C offers a range of additional benefits to the skin, such as promoting collagen formation and reducing dark-spot appearance.

These ingredients, taken orally, can help hydrate, rejuvenate, and protect skin for a more youthful appearance.

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Youthful Skin Begins Inside

Oral intake of certain plant-derived **nutrients** has been shown to support skin health and appearance.

Daily Skin Defense contains nutrients clinically studied to promote a:

3-fold improvement in skin moisturization

and

10-fold reduction in the appearance of wrinkle depth compared with placebo.[1]

Just one capsule of **Daily Skin Defense** provides:

- **Rice-derived ceramides** designed to help improve **skin moisture**.[2,3]
- **Four herbal extracts** to support the skin's barrier function against environmental factors and reduce appearance of **wrinkle depth**.[1]
- **Vitamin C** to support **collagen** production and improve the skin's natural protection against the oxidative stress caused by UV exposure.[4-6]

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ASHWAGANDHA'S Brain Benefits

BY RICK WILSON

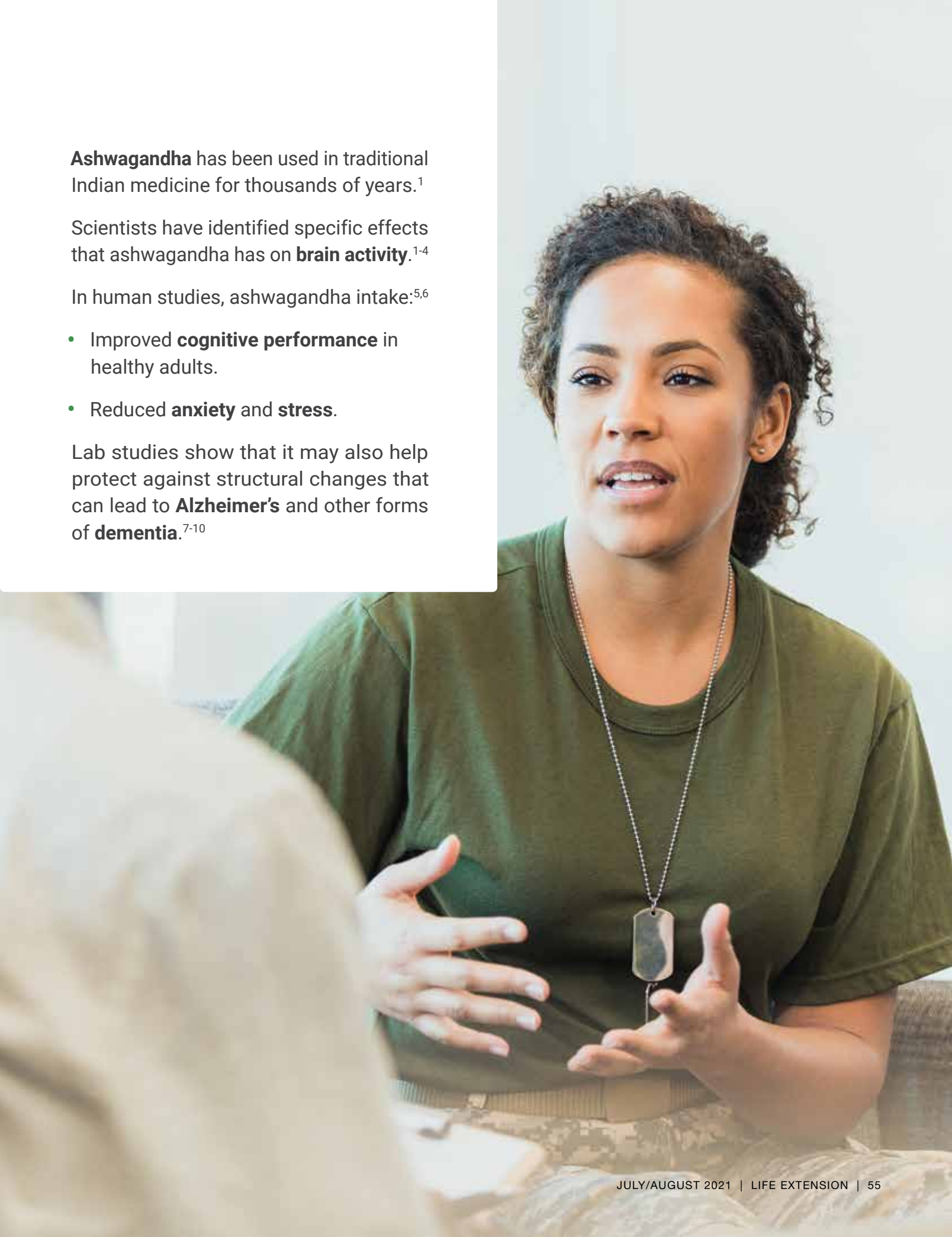
Ashwagandha has been used in traditional Indian medicine for thousands of years.[1]

Scientists have identified specific effects that ashwagandha has on **brain activity**.[1-4]

In human studies, ashwagandha intake:[5,6]

- Improved **cognitive performance** in healthy adults.
- Reduced **anxiety** and **stress**.

Lab studies show that it may also help protect against structural changes that can lead to **Alzheimer's** and other forms of **dementia**.[7-10]



A Staple of Ancient Medicine

Extracts of ashwagandha's roots and leaves contain a mixture of bioactive compounds, including **withaferin A**, **withanolides**, **withanosides**, and others.[2]

These compounds function as **antioxidants** and **anti-inflammatory** agents. They also act in other ways to protect the **brain** from disease.

They cross the **blood-brain barrier** and enter brain tissue, where they can exert beneficial actions.[11,12]

In healthy adults, ashwagandha taken daily has been shown to ***improve cognitive performance***—with boosts in reaction time, discrimination, vigilance, and other tests of brain function.[5]

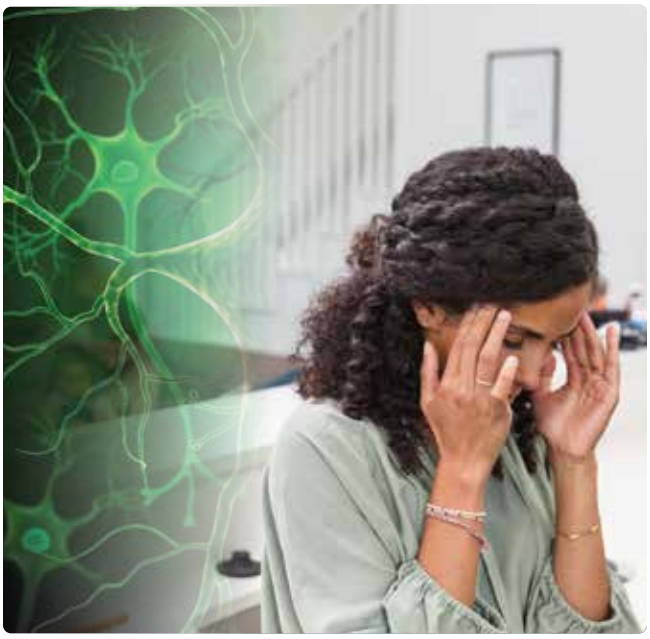
Relieving Anxiety and Depression

Nearly **10%** of American adults suffer from **mood disorders** like anxiety, depression, and bipolar disorder in any given year.[13]

Stress and anxiety are often treated with **drugs** that stimulate the receptor for a neurotransmitter called **GABA (gamma aminobutyric acid)**. These drugs have side effects, including fatigue and cognitive impairment.

Ashwagandha stimulates these *same* GABA receptors, *without* the side effects.[14,15] Rather than causing fatigue or cognitive impairment, ashwagandha is known to *enhance* cognitive performance.[5]

Ashwagandha has long been used to reduce stress and support a healthy mood.[14] A review of human trials found that it **improved anxiety** symptoms, compared to a placebo.[6]



In animal models of **depression**, ashwagandha extracts *reverse* signs of behavioral despair and other abnormalities and improve cognitive function.[16-19]

In two studies in rodents, the magnitude of this impact was comparable to the effects of **imipramine** and **fluoxetine** (Prozac®), two drugs used in humans to treat depression and other disorders.[16,17]

In patients with schizophrenia, who are prone to ***anxiety and depression***, an ashwagandha extract reduced symptoms of *both*.[20]

Protecting Brain Cells

Ashwagandha may protect against various forms of **dementia**.

In laboratory studies of animal models of **Alzheimer's disease**, ashwagandha displays various mechanisms known to reduce its progression.

One of the primary features of Alzheimer's is the accumulation of an abnormal protein called **beta-amyloid**.

This buildup inflicts toxic effects on brain cells and incites aggressive chronic inflammation, which leads to further deterioration of brain function.

Preclinical studies have shown that ashwagandha:

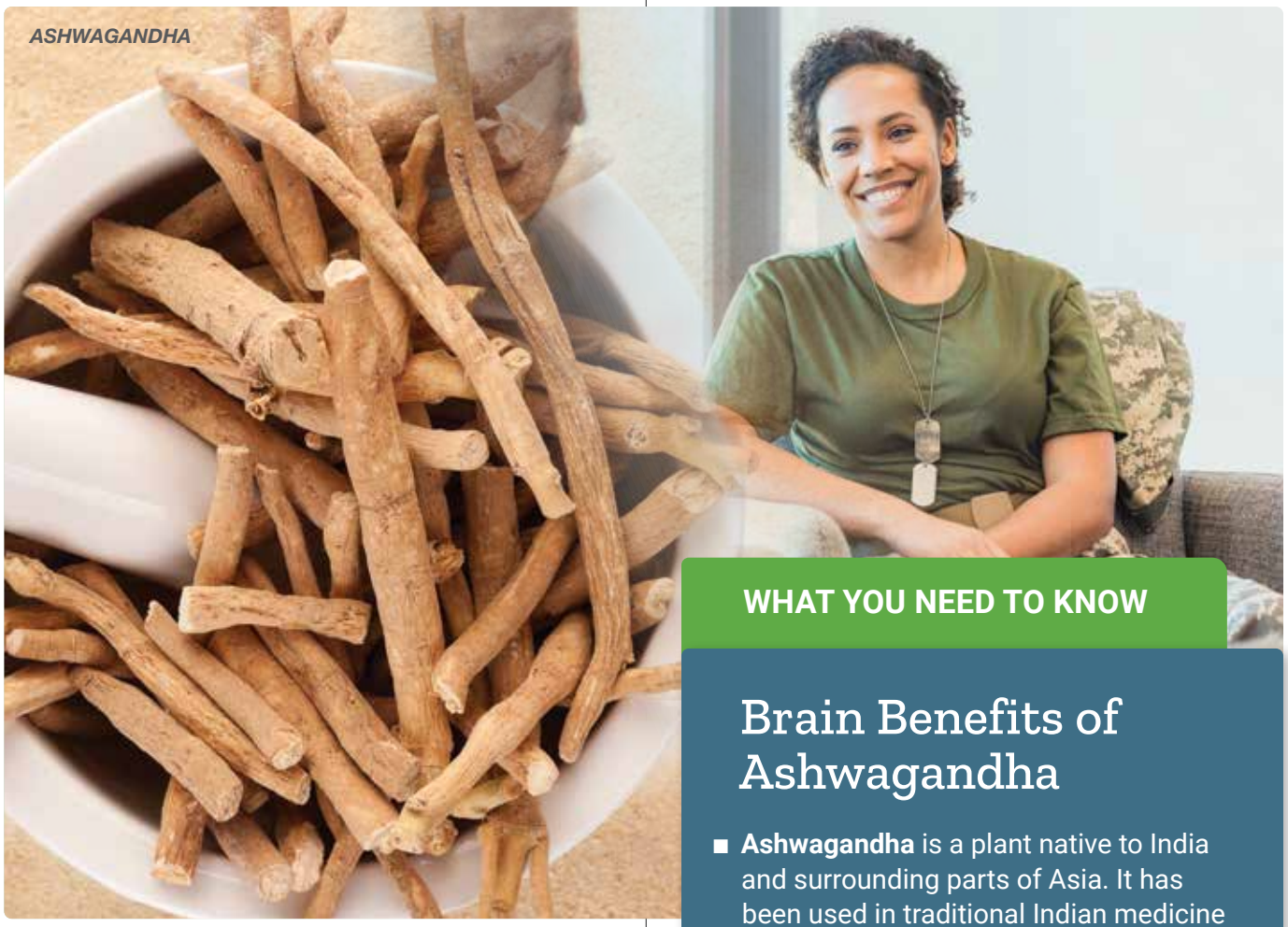
- Reduces the *formation* of amyloid in the brain and brain cells,[21,22]
- Prevents the *accumulation* and aggregation of amyloid,[23]
- Reduces the *toxic impact* of existing amyloid, protecting brain cells from injury and inflammation, and[21,22,24]
- Aids in *removing* existing amyloid deposits, *reversing* Alzheimer's disease pathology.[25]

Animal models of Alzheimer's also show a drop in two key proteins associated with brain maintenance and repair: **brain-derived neurotrophic factor (BDNF)** and **glial fibrillary acidic protein (GFAP)**. Ashwagandha helps maintain *higher* levels of both these protective proteins.[26,27]

Boosting Acetylcholine

One effect of memory loss caused by Alzheimer's disease is a loss of **acetylcholine** function.

Acetylcholine is a neurotransmitter used for cell-to-cell communication in the brain. It is vital to normal cognitive function.



Some medications used to treat Alzheimer's *inhibit* the enzyme that breaks down acetylcholine, boosting its levels. Ashwagandha also blocks this enzyme, increasing acetylcholine levels.[8-10]

Together, these actions suggest that ashwagandha could help fight some of the primary damage that is among the causes of Alzheimer's disease, while also supporting healthy brain function.

Ashwagandha has also shown promise in preclinical studies of other neurodegenerative diseases, including Parkinson's disease, amyotrophic lateral sclerosis (ALS), and Huntington's disease.[1,2,28,29]

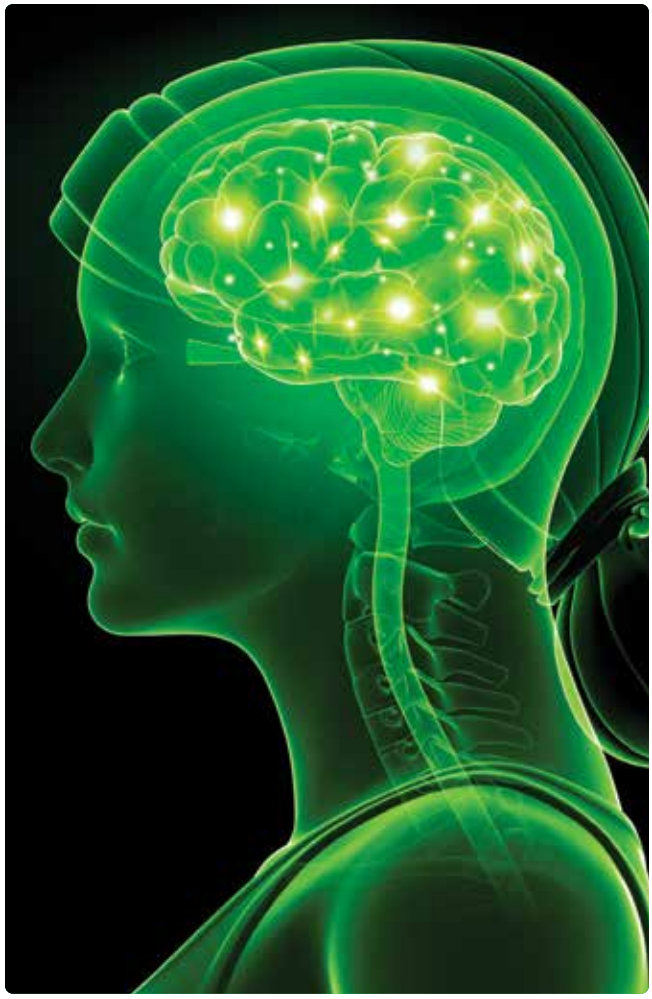
Defense Against Neurotoxins

Ashwagandha has been found, in preclinical models, to shield against a range of neurotoxins, including lead, aluminum chloride, streptozotocin, scopolamine, kainic acid, and bisphenol A (**BPA**, a common additive in plastics).[1,30,31]

WHAT YOU NEED TO KNOW

Brain Benefits of Ashwagandha

- **Ashwagandha** is a plant native to India and surrounding parts of Asia. It has been used in traditional Indian medicine for millennia to promote overall health.
- Modern science has found that ashwagandha promotes healthy functioning of the **brain**.
- Extracts of ashwagandha may protect the brain from damage caused by a wide range of **toxins**, injuries, and **stroke**.
- Oral intake improves **cognitive performance** in healthy adults and in those with signs of cognitive decline.
- Ashwagandha reduces stress and anxiety, and relieves symptoms of depression.
- Research shows that ashwagandha may help protect against forms of dementia, including **Alzheimer's disease**.



One example is **glutamate**. Glutamate is an amino acid that acts as a neurotransmitter in the brain. Normal levels of glutamate are vital to brain communication.[4]

But very *high* levels of glutamate can cause **excitotoxicity**—overstimulation of brain cells that can cause them to go haywire, and even die. Some brain injuries, such as **traumatic head injuries** and **stroke**, cause a huge release of glutamate that results in further cell death.[4]

Glutamate excitotoxicity has been found to be a component of the pathology seen in neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, ALS, and multiple sclerosis.[4]

Ashwagandha defends the brain against this damage. In lab studies, pretreatment with ashwagandha extracts *before* exposure to high levels of glutamate markedly **inhibit cell death** and other changes associated with excitotoxicity.[1,32,33]

Helping Stroke Victims

The most common forms of **stroke** result from a lack of oxygen and blood to the brain, leading to cell dysfunction and death.

In several animal studies of experimental stroke, **ashwagandha** intake prevented much of this brain damage.[34-38] It reduced the size of the brain injury and the biochemical changes that typically accompany stroke.

This helped prevent the behavioral, motor, and cognitive dysfunction that would otherwise have occurred.

These actions, along with its other benefits, make **ashwagandha** a powerful neuroprotective nutrient.

Summary

The herb **ashwagandha** has been used for its diverse health benefits for thousands of years.

Ashwagandha extract appears to be beneficial to the **brain**.

It may shield the brain from damage resulting from exposure to **toxins**, physical injury, and **stroke**.

It helps relieve stress and improves symptoms of **anxiety** and **depression**.

Ashwagandha also improves **cognitive performance** and may defend against cognitive decline and dementia. •

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ADDITIONAL BRAIN-BOOSTING NUTRIENTS

SAGE

Researchers have identified a unique form of sage that improves cognitive function.

Clinical evidence demonstrated that this proprietary extract increased **memory performance** in older adults by nearly **60%** and improved **attention** by **250%**—*within hours* of ingestion.[39]

In addition to enhancing **cognitive function** in humans, this unique **sage extract** has been shown to increase **lifespan** by **12%** in a *C. elegans* model of aging.[40]

PHOSPHATIDYLSERINE

Phosphatidylserine is a **phospholipid**, one of the structural components of the membranes that surround all cells in the body.[41,42] This is especially critical for nerve cells in the brain, because it is their cell membranes that carry nerve impulses throughout the nervous system.[43] The **myelin** that surrounds nerve fibers and aids signal conduction also relies on phosphatidylserine for normal structure and function.

Aging is associated with structural deterioration in the nervous system, which may be reduced by phosphatidylserine's ability to preserve cognitive function.

BLUEBERRY

Blueberries are packed full of **anthocyanins**, powerful compounds that help protect the plant from oxidative stress. These compounds have been explored in the medical literature for years for their potential health benefits to humans.

Several recent trials in humans have demonstrated that blueberries enhance cognitive function. Not only has blueberry been found to enhance memory and other cognitive performance in older subjects, it improves mood and cognition in children and young adults as well.[44-48]

PREGNENOLONE

Pregnenolone, a hormone and hormone-precursor, as well as the derivatives it forms in the brain, have modulatory effects on nervous system function.

Several studies in animals and humans have reported beneficial effects for the brain.[49]

Pregnenolone appears to be a neuroprotectant, defending the brain from various forms of injury. It has also been found to have positive effects on mood, memory, and other aspects of cognition.

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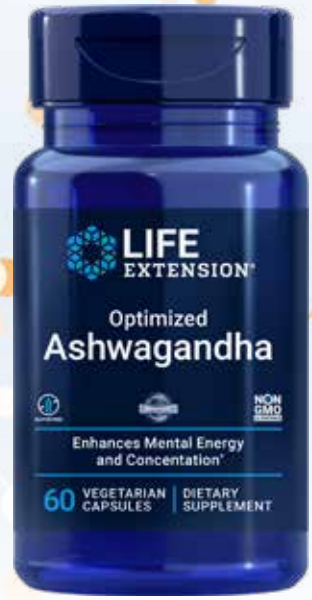

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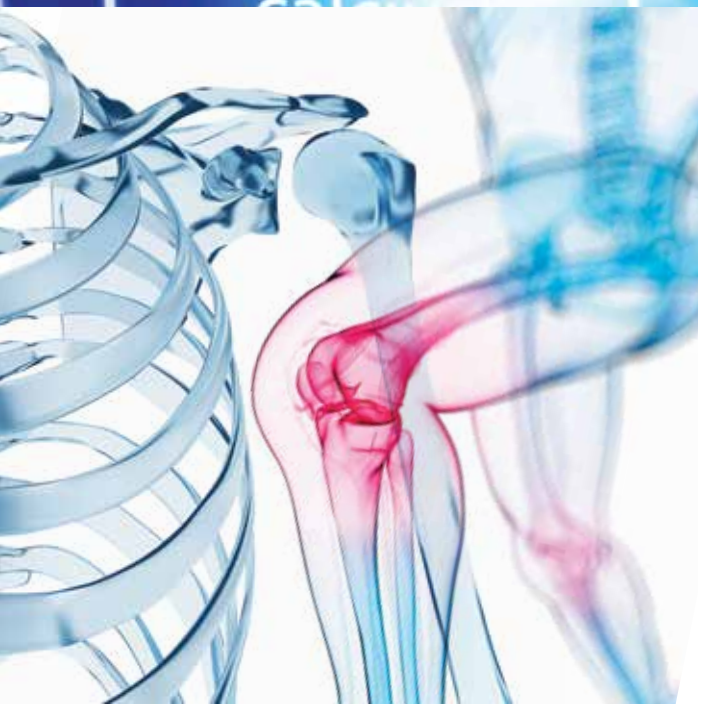
The VITAMIN D-MAGNESIUM Connection

BY MARSHA MCCULLOCH, RD



The use of **vitamin D** has grown substantially over the past decade.[1]

That's for good reason. Vitamin D is essential for immune function, heart health, and cognitive performance.[2,3]

Unfortunately, many people aren't getting the *full* benefits of vitamin D because they have a low level of **magnesium**.

Researchers have documented the essential relationship between magnesium and vitamin D.[4]

It's estimated that **45%** of Americans are magnesium deficient.[5]

Magnesium is ***essential*** for converting vitamin D into its **active** form in the body.[6,7] Magnesium also aids vitamin D **transport** in the blood.[8,9]

At the same time, maintaining sufficient levels of vitamin D helps magnesium achieve *its* many benefits.[10-12]

A growing number of human studies focusing on the use of both vitamin D and magnesium are confirming their combined benefits for immunity, muscle strength, heart health, and more.[13-15]

The Importance of Vitamin D and Magnesium

Vitamin D and the mineral **magnesium** each have well-known health benefits.

Low levels of **vitamin D** can lead to weak bones, along with increased risk for cardiovascular disease, metabolic disorders, and cognitive decline.[16-18]

Magnesium deficiency can result in muscle spasms and cramps.[19] Low magnesium can also contribute to osteoporosis, irregular heart rhythms, and migraines.[20]

Oral intake of vitamin D and magnesium, *individually*, can help treat or lower risk for many of the same health concerns. These include:[2,8,9,20,21]

- Musculoskeletal disorders,
- Type II diabetes,
- Cardiovascular disease,
- Some cancers,
- Immune system problems, and
- Neurological conditions, such as depression and dementia.

But for vitamin D and magnesium to work *optimally*, they need each other.

Magnesium Activates Vitamin D

Vitamin D consumed orally or made in the skin from sun exposure is **inactive**.[10]

This is also true of both vitamin **D2**, which is obtained from plant sources, and vitamin **D3**, which is made in the skin or found in oily fish and eggs.[22]

Before vitamin D can perform its vital functions, it must be activated by a two-step process:[10,23-25]

In the **liver**, an enzyme called *25-hydroxylase* converts vitamin D2 and D3 to **25-hydroxyvitamin D**. This is the major *circulating* form of vitamin D measured in blood tests to assess vitamin D levels.

In the **kidneys** (and other tissues) another enzyme, *1-alpha-hydroxylase*, converts 25-hydroxyvitamin D into active **vitamin D**.

Both of these enzymes ***need magnesium*** to function properly.[6,7] Otherwise, vitamin D will remain in its *inactive* form, making it all but useless.

Magnesium also regulates **24-hydroxylase**, an enzyme that helps *inactivate* vitamin D when there's an *excess* supply.[4,6]

Transport and Regulation of Vitamin D

Magnesium enables vitamin D to bind to a **carrier protein** that transports it though the blood.[6,8]

Then, when active vitamin D arrives where it is needed, magnesium helps activate the **receptors** needed for cells to use vitamin D.[20]

Magnesium deficiency *decreases* the number of vitamin D receptors in cells, limiting the vitamin's effects.[20] Aging leads to a decrease in vitamin D receptors.[26]

Magnesium also boosts vitamin D activity by supporting synthesis and secretion of **parathyroid hormone**.[4,8,10,11] This hormone stimulates the kidneys to convert vitamin D to its active form.[22]

Vitamin D's Impact on Magnesium

The magnesium-vitamin D partnership isn't a one-way street.

Vitamin D can enhance intestinal **absorption** of magnesium, particularly in people with low magnesium levels.[10-12] This allows the mineral to be more efficiently used by the body.

In one human study, obese women given a **vitamin D** injection had a significant *increase* in their blood levels of **magnesium**.[12]

A Life-Saving Partnership

The link between vitamin D and magnesium can be seen in studies of **longevity**.

Vitamin D *deficiency* is known to be associated with a *higher* risk of death. In a large observational study, low **magnesium** levels made that risk even greater.[27]

In this study, 1,892 men (ages 42-60 years) were followed for an average of 22 years.

In men with low vitamin D levels, a ***lower magnesium*** intake (less than **414 mg** per day) was associated with ***a 60% greater risk of death*** than for those with a *higher* magnesium intake.[27]

Further evidence of the link between the two nutrients comes from human studies of **rickets**, a softening or weakening of bones caused by severe and prolonged vitamin D deficiency.

In these studies, vitamin D intake *alone* failed to treat rickets. But adding **magnesium** to the regimen supported vitamin D activation and helped resolve the condition.[4]

In another recent study, 27 healthy, postmenopausal women were given **500 mg** of **magnesium** daily for two months, while 25 matched women received **placebo**. Most of the women were vitamin D deficient, and many were low in some measures of magnesium.

This study showed that in response to magnesium supplementation (with no vitamin D), the number of women deficient in **vitamin D** decreased by about **20%**.[28]

Bone and Teeth Health

Both vitamin D and magnesium are important for healthy **bone mass** and **strength**.[19,29]

Together, they are even more beneficial. Vitamin D promotes intestinal absorption of calcium and magnesium, which are vital components of bone that help prevent **osteoporosis**.

Insufficient magnesium can impair bone health by causing a reduction in **parathyroid hormone** levels and a *decrease* in active vitamin D levels.[11]

Vitamin D and magnesium also play key roles in replenishing the minerals in teeth. This may help prevent **tooth loss**.[29,30]

Optimizing vitamin D intake also promotes the success of **dental implant** surgery, an increasingly popular option for replacing missing teeth.[31]

Oral health has a wide impact on whole-body health due to the association between **periodontal disease** (gum inflammation) and **systemic disease**, including type II diabetes and cardiovascular disease.[30]

Vitamin D and magnesium help combat oral inflammation to *prevent* periodontal disease.[29,32]

WHAT YOU NEED TO KNOW

Vitamin D and Magnesium: Partners in Health

- The **vitamin D** produced from sun exposure and consumed in food or through direct oral intake is **inactive**.
- Enzymes that **activate** vitamin D require the mineral **magnesium** to work properly. Magnesium also supports the transport of vitamin D throughout the body.
- Vitamin D can enhance magnesium **absorption** in the intestines.
- By working in partnership, magnesium and vitamin D support musculoskeletal and heart health and promote proper metabolic function.

Muscle Strength and Function

One of the most significant challenges in aging is **sarcopenia**, the loss of muscle mass, strength, and function. It frequently leads to falls and fractures in older adults.[33]

Chronic inflammation is one contributor to sarcopenia. Vitamin D and magnesium can help *reduce* inflammation and may *prevent* sarcopenia.[14]

Scientists have discovered that **muscles** have receptors for vitamin D. As people age, these tend to decline in number. Taking oral vitamin D *increases* the number of receptors in muscle tissue.[34]

In a study of 83 healthy, middle-aged women deficient in vitamin D, half the group received **50,000 IU** of **vitamin D** weekly and **250 mg** of **magnesium** daily for eight weeks. The rest of the group received placebos.

Women who received the vitamin D and magnesium had a significant *increase* in **handgrip strength** and overall **mobility**, compared to the placebo group. The treatment group also had a *decrease* in an important inflammatory marker, compared to the beginning of the study.[14]

Cardiometabolic Health

In observational studies, *higher* intake and blood levels of both vitamin D and magnesium have been linked with a *lower* risk of **insulin resistance** and **type II diabetes**.[35,36]

Vitamin D appears to improve **insulin secretion** from the pancreas, which has specific receptors for interacting with the vitamin.[35] Magnesium also supports insulin secretion.[37]

Magnesium plays an important role in protecting cells from **oxidative stress** as well. Magnesium deficiency results in *decreased* production of **glutathione**, one of the body's most potent antioxidants.[37]

Multiple studies conducted across several decades show that magnesium and vitamin D intake interacted in affecting vitamin D status.[4,38,39]

The vitamin and mineral intake also interacted with circulating vitamin D levels in the risk of cardiovascular mortality.[4,6]

Without enough magnesium and vitamin D, calcium isn't properly routed to the bones. Instead, calcium is more likely to deposit in arteries, increasing risk of **cardiovascular disease**.[11,40]

Summary

The health benefits of **vitamin D** are well-established. But the *effectiveness* of vitamin D intake depends on getting enough **magnesium**, a nutrient on which nearly **half** of all Americans fall short.

The body needs magnesium to **activate** and **transport** vitamin D. In return, vitamin D can *enhance* magnesium **absorption** and retention.

Working together, magnesium and vitamin D can benefit musculoskeletal, metabolic, and heart health.

Vitamin D and **magnesium** are clearly both vital for overall health. Taking one without the other fails to take advantage of their full benefits. •

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* **EGCG** is the acronym for **epigallocatechin gallate**, which is the polyphenol in green tea that has demonstrated the most robust health benefits.

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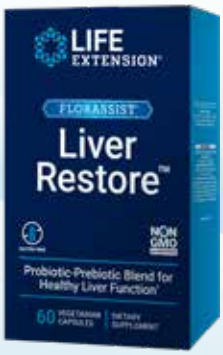

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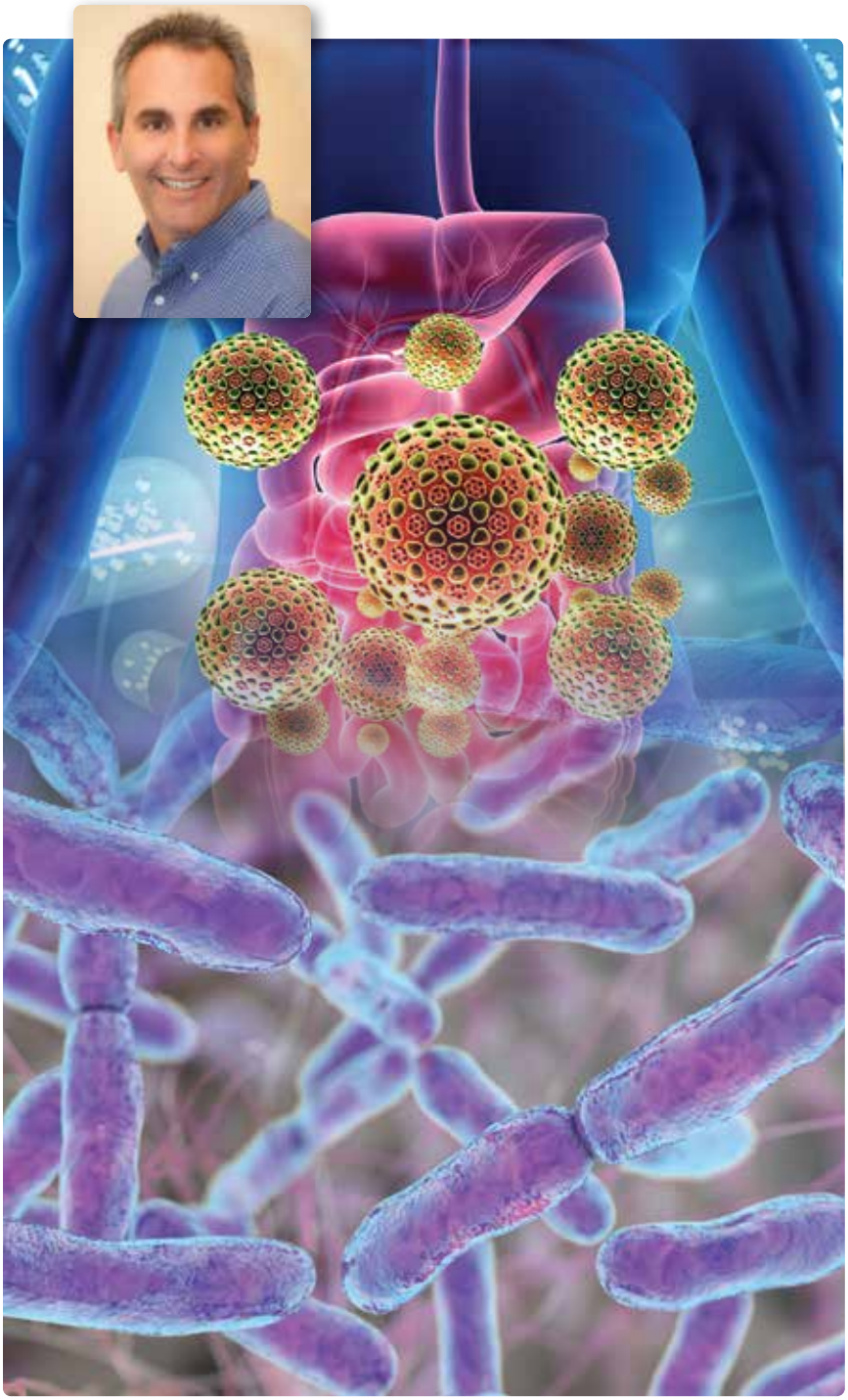
Understanding Probiotics

BY ANDREW SWICK, MS, PhD



Scientific research has shown a wide range of benefits for **probiotics** in recent years.

As a result, there's now a glut of products on the market with probiotics added to them, from dietary supplements to breakfast cereals.

But probiotics aren't all the same, and it's important to take ones that have been tested and verified as effective in scientific studies.

In this interview with ***Life Extension®***, **Dr. Andrew Swick** talks about the benefits of different probiotic strains, how you can ensure you're getting the right kinds, and more.

LE: **Probiotics** are very popular now. What exactly are they?

Dr. Swick: Probiotics are live microorganisms that provide health benefits when consumed in appropriate amounts. The majority of probiotics are **healthy bacteria**. These "good" bacteria are beneficial in many ways, including some that help fight off "bad" bacteria. Probiotics take part in the larger community of microorganisms that live in many areas of your body, including your gut, skin, and mouth. This larger community is most commonly referred to as your "**microbiome**."

LE: People often hear that fermented foods like yogurt contain probiotics. Is that correct?

Dr. Swick: Yogurt and other fermented foods, including kefir, kimchi, kombucha, sauerkraut, and pickles, *do* contain live microbes. These active cultures are popularly referred to as probiotics. But while these foods may provide some health benefits, they don't always meet the strict **scientific definition** of probiotics.

The International Scientific Association for Probiotics and Prebiotics (ISAPP) only designates **strains** that have been *characterized* (properly identified and named), scientifically studied, and demonstrated to provide health benefits, as **probiotics**. Fermented foods contain mixtures of microbes that are for the most part *uncharacterized*, and may not meet the level of scientific evidence required by the ISAPP to be considered probiotics.

LE: You mentioned strains. What are those and how do consumers know if they are getting the correct strain?

Dr. Swick: Consumers should look at the *full* name of each probiotic listed on a product label. Each probiotic has three names in the following order: **genus**, **species**, and **strain**. For example: In ***Lactobacillus rhamnosus* CRL1505**, *Lactobacillus* is the genus, *rhamnosus* is the species, and CRL 1505 is the strain.

Consumers sometimes overlook the **strain**, but it's very important. The specific strain is what was studied to determine the health benefits associated with the probiotic. Strains are not interchangeable, and they have specific benefits.

Think of it like this: All dogs are the same genus and species, *Canis familiaris*. But different breeds may

be nothing alike. For bacteria, **strain** can be thought of as the breed. Not knowing the strain would be like adopting a dog without knowing the breed. A Chihuahua is very different from a Great Dane!

LE: Probiotics sold as dietary supplements may contain different amounts of **colony forming units** (**CFUs**), as well as a variety of strains. Is more always better?

Dr. Swick: No. That's a common misconception. The **amount** and **specific** strains listed on the label should be consistent with what was tested in a study. A larger amount or number of probiotic strains does not mean it's more effective.

LE: People mostly think of probiotics as helping with **digestive** health. But now there are targeted probiotics that can improve conditions as varied such as gum disease, depression, and allergies. How do these work?

Dr. Swick: Initially, probiotics were thought to be beneficial only for gastrointestinal health. We now know that specific strains of probiotics are helpful for a variety of conditions. Specific strains have been clinically demonstrated to support a healthy heart, throat, immune response, liver, and even mood.

In general, **condition-specific probiotics** work by supporting an overall healthier microbiome, producing substances that have specific effects,[1] and beneficially influencing immune responses. Targeted probiotics present a meaningful advance for supporting disease prevention and health.

LE: Can you give some examples of specific strains and the conditions they benefit?

Dr. Swick: Many human mouths are teeming with a type of bacteria, *Streptococcus mutans*, that is a cause of cavities, gingivitis (gum inflammation), and

periodontitis (gum disease).[2] Nearly a **third** of U.S. adults have untreated tooth decay, and nearly **half** of those 30 and older have periodontal disease.

In a clinical study, scientists demonstrated that ***Streptococcus salivarius* M18** was able to decrease the plaque index score and improve other measures of oral health. This is particularly important since we now know that gum disease is associated with other health conditions, including heart disease.

Another interesting application of condition-specific probiotics is in mitigating **depression** and **anxiety**. In two randomized controlled trials, participants taking a blend of ***Lactobacillus helveticus* Rosell-52** and ***Bifidobacterium longum* Rosell-175** reported significant improvements in mood, stress response, and emotional balance. One human study showed a **50%** improvement in depression scores with these two probiotics, and another showed a **55%** improvement in anxiety scores.[3,4] The connection between the gut and brain is an exciting area of active research.

Scientists have also discovered and characterized a probiotic, ***Lactobacillus rhamnosus* CRL 1505**, that stimulates the **immune system** in the respiratory tract and gut. In clinical studies, administration of this probiotic strain led to reduction in infection symptoms, infection incidence, and use of antibiotics. The data were so compelling that *Lactobacillus rhamnosus* CRL 1505 was provided to schoolchildren as part of a national nutrition program in Argentina.

As research continues, new targeted probiotics are being developed for conditions such as constipation, and to support longevity.

LE: We also hear a lot lately about prebiotics. What are those?

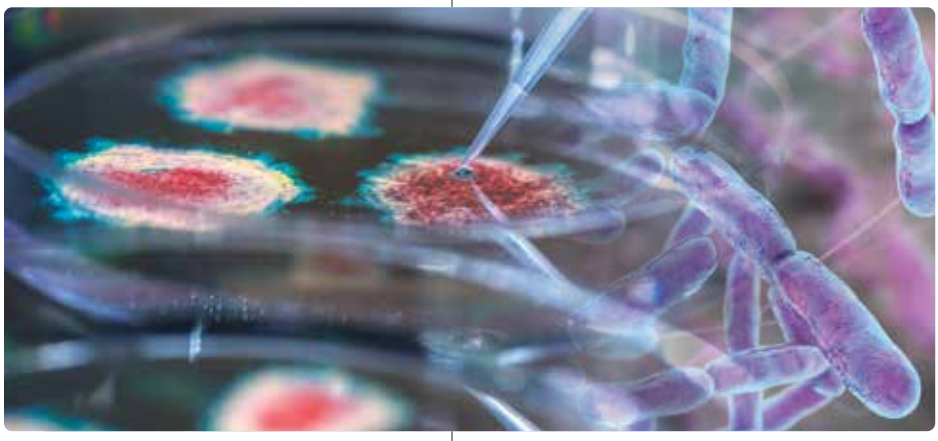
Dr. Swick: Prebiotics are basically compounds that serve as "food" to support the growth of probiotics. Most prebiotics are dietary fibers, but not all dietary fibers are considered to be prebiotics.

LE: You've given us a lot of information. Can you provide the reader with some simple guidelines about how to select appropriate probiotic products?

Dr. Swick: Choosing a probiotic can be overwhelming! Here are a few key points to remember:

1. First and foremost, only purchase probiotics that are high quality and backed by science.
2. Ensure that the strain is clearly identified and appropriate for the specific conditions you want to address.
3. Remember that more is not better. The CFUs should be consistent with what was clinically studied.

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. Swick is the Chief Scientific Officer for **Life Extension**® and oversees all scientific and product development initiatives. Immediately prior, Dr. Swick was the Vice President of Nutrition Science at Metagenics. Dr. Swick also has deep pharmaceutical industry experience, having performed both scientific and managerial roles at Pfizer for more than 17 years, where he was responsible for drug discovery and research for obesity and atherosclerosis. Previously, he also served as an Associate Professor at the Nutrition Research Institute at the University of North Carolina at Chapel Hill. Dr. Swick earned his PhD in Nutritional Biochemistry from the University of Wisconsin-Madison and was a Postdoctoral Research Fellow at the Johns Hopkins University School of Medicine and University of North Carolina Lineberger Comprehensive Cancer Center.

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FISETIN

The Longevity Flavonoid

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]
- Inhibits excess **mTOR** activation[8]

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

Bio-Fisetin supports against this breakdown 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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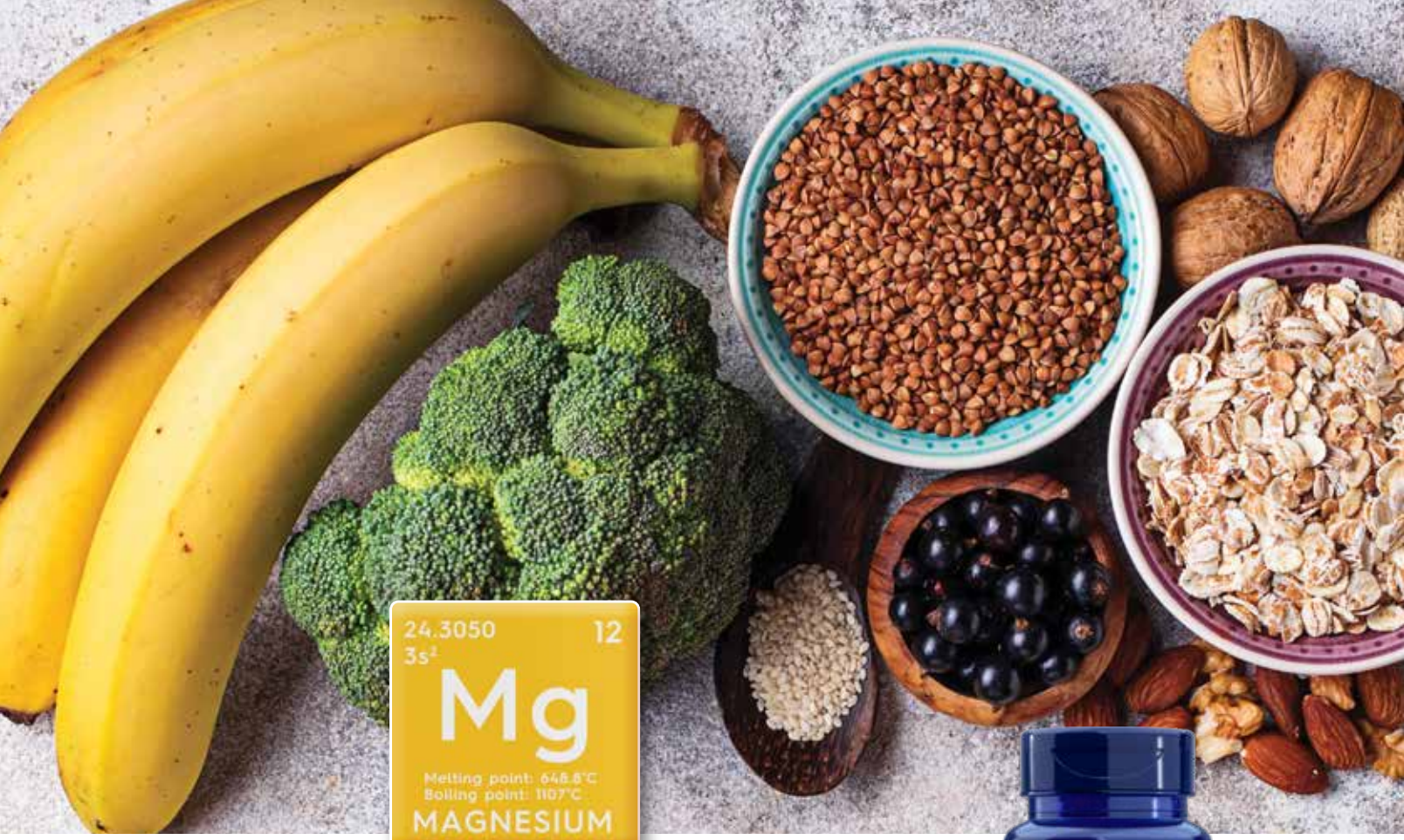

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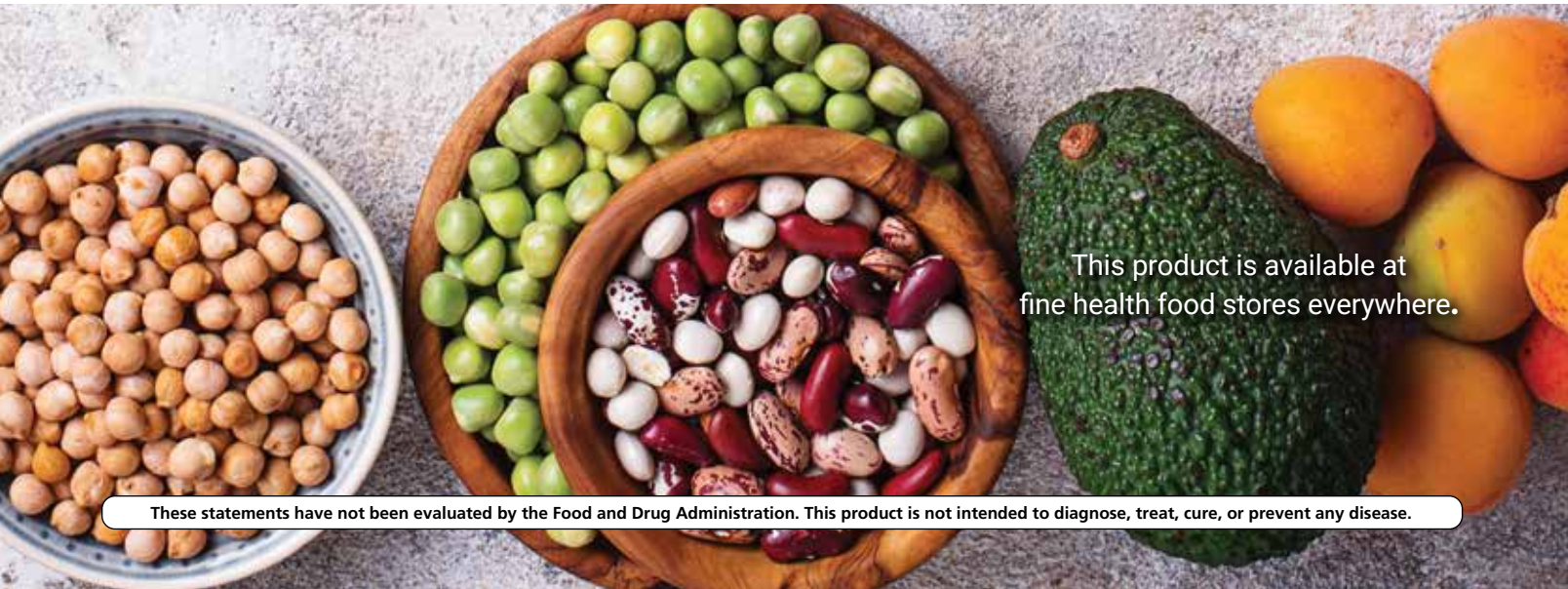

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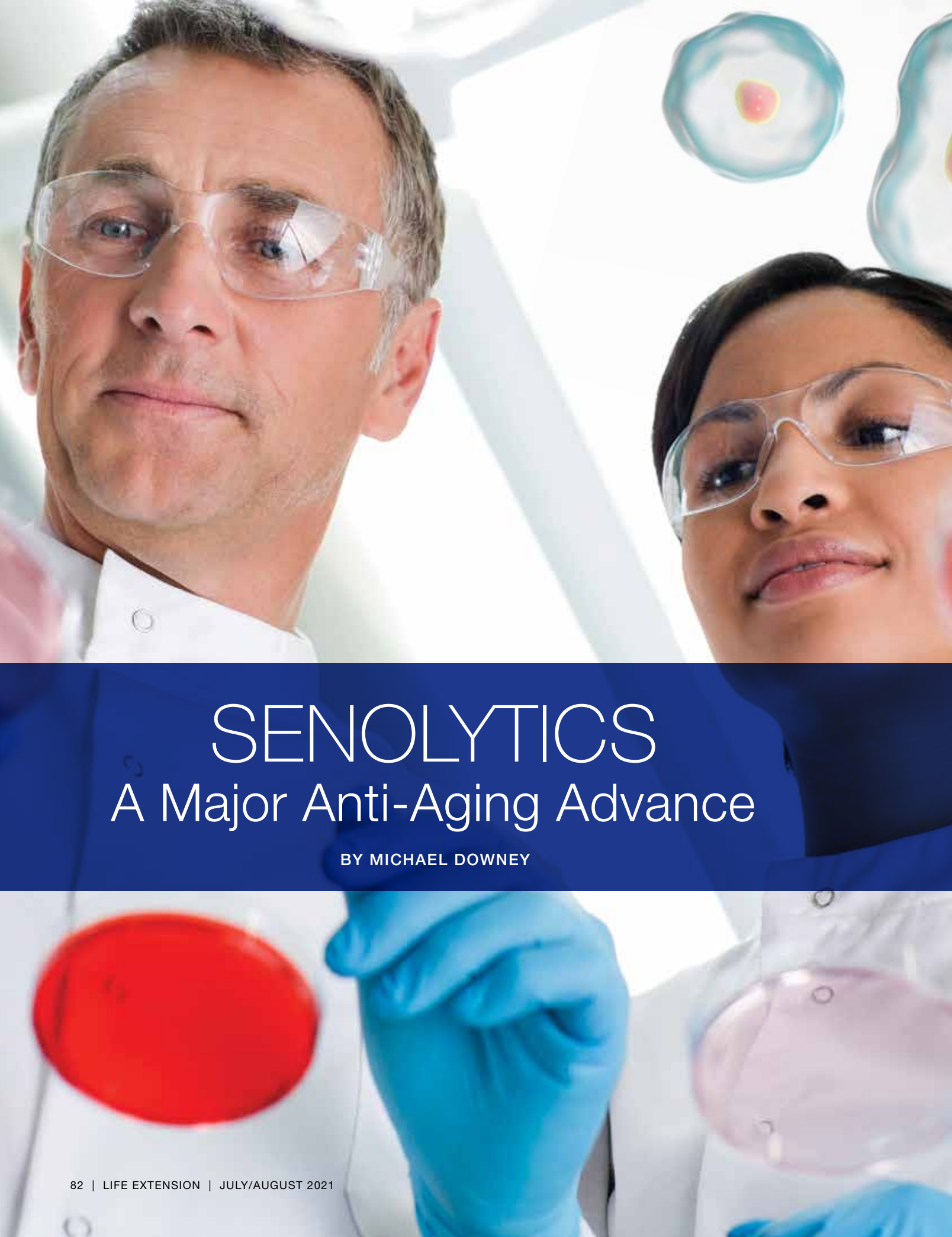
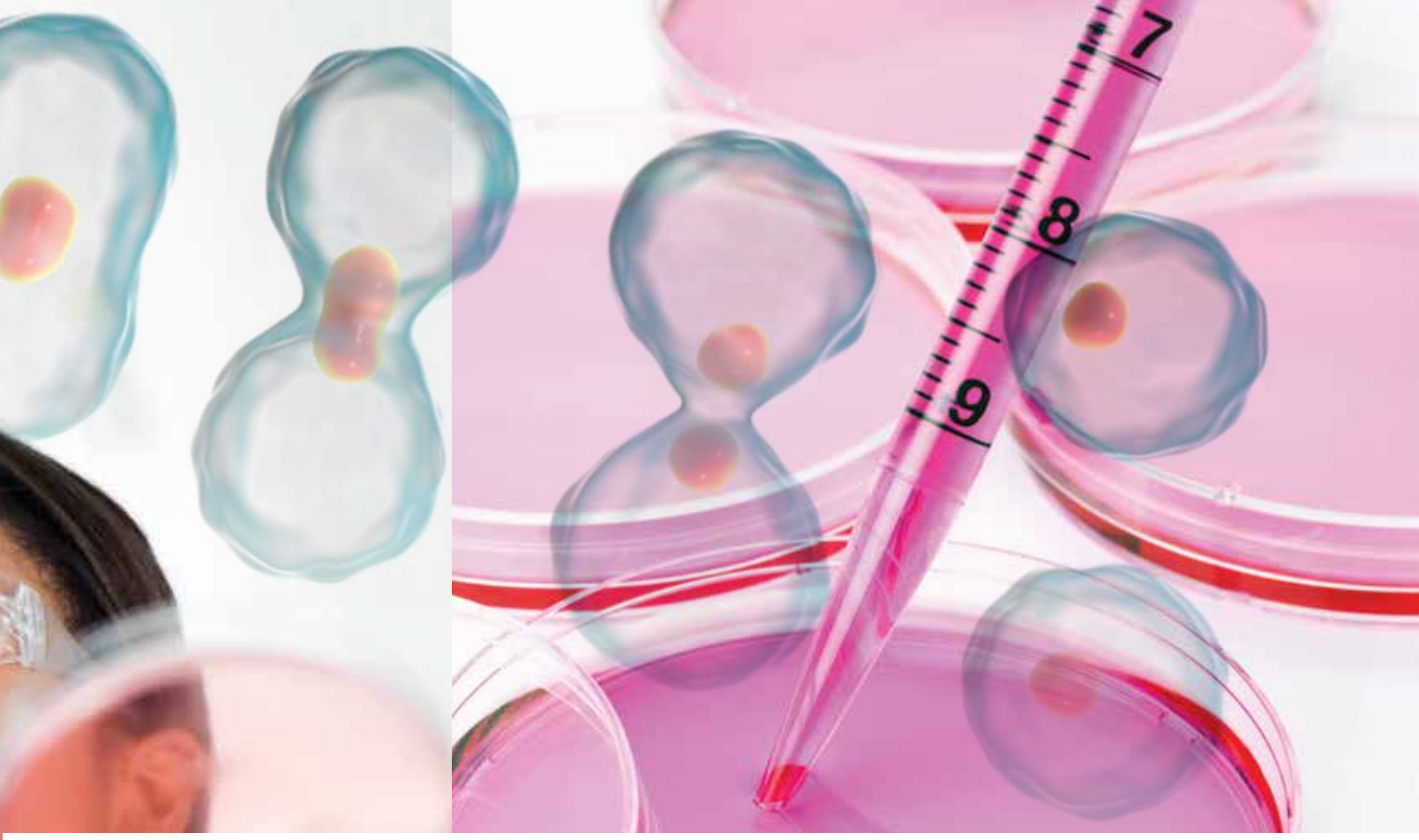


SENOLYTICS
A Major Anti-Aging Advance

BY MICHAEL DOWNEY



When old cells become dysfunctional, they're supposed to die off through a normal process called apoptosis.

But as we age, we accumulate too many of these malfunctioning (senescent) cells that refuse to die.

Sometimes referred to as "zombie cells," they pump out toxic compounds that degrade nearby cells and incite **chronic inflammation** that inflicts systemic damage.[1]

Compounds called **senolytics** *remove* senescent cells. Preclinical studies show that they can slow or ***reverse*** certain aspects of ***aging***.[2-5]

Nutrients like **quercetin** and **theaflavins** (from black tea) have demonstrated **senolytic activities** and have been widely used in recent years.

The plant flavonoid **fisetin** is currently considered one of ***the most powerful natural senolytics***.[4,6-20]

Its effects are dramatic. Elderly mice given **fisetin** had their ***lifespans extended by nearly 10%***.[4] This may be analogous to a **75-year**-old human living about **7.5 years** longer.

The challenge up until now was that **fisetin** is converted into other compounds in the digestive tract. This means very little whole, unaltered fisetin is ***absorbed*** into the bloodstream.

Scientists have developed a method to increase **fisetin** blood levels up to **25 times** higher,[21] thus enabling **fisetin** to be distributed throughout the body.

Enligthened individuals today are taking this highly-absorbable **fisetin** by itself and/or combining it with a once-weekly high potency **quercetin + theaflavins** for enhanced **senolytic** effects.

Senescent Cells and Aging

In youth, cells naturally eliminate themselves if they become damaged or dysfunctional. This process is called **apoptosis**.[22]

With age, however, we accumulate more **senescent cells** that emit toxic byproducts, that cause more cells to become senescent. These dysfunctional cells no longer perform basic functions. They instead inflict localized and systemic damage to our healthy cells.

Senescent cells undergo a series of transformations that result in their **secreting** high levels of **toxic compounds,** collectively referred to as **SASP** or **senescence-associated secretory phenotype**.

As a result, the buildup of **senescent** cells has been shown to ***accelerate the aging process*** and increase the risk of age-related diseases, including:[23-30]

- Diabetes,
- Obesity,
- Stroke,
- Vision loss,
- Neurodegenerative disorders,
- Osteoarthritis,
- Emphysema, and
- Cancer.

Research shows that just **one** senescent cell out of **7,000-15,000** healthy cells can initiate degenerative aging.[31]

Removing **senescent** cells from the body can *reduce* the cellular drivers of aging and improve overall health.[32]

That's where **senolytics** come in.

Senolytics to the Rescue

Senolytics are compounds that enable the body to remove **senescent** cells.[33,34]

They work by ***reactivating*** the apoptosis switch in senescent cells. That causes these toxic cells to die and make room for healthy young cells.[35]

Published scientific studies demonstrate that *removing* senescent cells from the body improves markers of aging and prolongs lifespan in some models.[28,32,33,35,36]

In mice with **atherosclerosis**, removing senescent cells significantly inhibited the growth of arterial plaque and even caused it to regress.[37] This could be an important step in preventing heart and blood vessel disease.

In another study, a mouse model of **aging** showed that removing senescent cells benefited multiple tissues, while *delaying* the onset and slowing the progression of age-related disorders.[28]

Fisetin: Today's Ultimate Senolytic

Scientists have studied many different nutrients, searching for effective **senolytics**.

Fisetin is the ***most potent "on target" senolytic*** known today.[4]

Fisetin is a flavonoid found in small amounts in strawberries, apples, persimmons, grapes, onions, and other plants. A cell study found that it eliminated about **70%** of senescent cells—while doing *no harm* to healthy human cells.[5]

These and other effects of fisetin have been shown to increase **longevity** in various animal models.[2,15]

Mice given fisetin lived an average of about 2.5 months longer, an almost **10% extension of lifespan**—even when treatment started at the **human** equivalent of **75 years** of age.[4]

Other Benefits of Fisetin

The effects of **fisetin** go beyond its potent **senolytic** activity.

Fisetin also:

- Protects the **brain** in various models of neurodegenerative disorders,[6-8,13-15,20]

- Improves outcomes in people who have suffered **strokes**,[18]
- Helps prevent **malignant** changes inside cells, [11,12,16,19]
- In animal and experimental models, helps fight **obesity** and **type II diabetes** tendencies,[9,10,17]
- Reduces the risk of **atrial fibrillation** after a heart attack, in an animal study,[38]
- Reduces levels of **pro-inflammatory** mediators, in a study of colorectal patients,[39] and
- Based on results of preclinical studies, may inhibit cancer migration and growth and incite **cancer cell death**.[16,40-45]

Fisetin also has an ability to impact many of the same cellular pathways that **calorie restriction** does.[2,15,46,47] Reducing food intake through a **calorie-restricted diet** has been shown to slow aging, extend lifespan, and improve resistance to disease.[48]

Until recently, there's been a challenge with oral fisetin: It is rapidly converted into other compounds in the gut. Scientists have solved this problem by *combining* fisetin with a fiber called **galactomannans**, isolated from the spice **fenugreek**.

This formulation has been shown to increase the **bioavailability** (absorption) of fisetin by as much as **25 times**, greatly enhancing its impact.[21]

The Power of Quercetin

Before fisetin, quercetin, found in many fruits and vegetables, was one of the first plant-derived flavonoids to be tested as a senolytic.[49]

Quercetin has long been recognized for a range of benefits, including:

- Anti-inflammatory activity, shown to protect cells and tissues from injury,[50-54]
- Improved markers of aging and extended lifespan in lab studies,[55-60] and
- Reduction or prevention of age-related disease and dysfunction in human studies.[61,62]

WHAT YOU NEED TO KNOW

Removing Senescent Cells for Better Health

- With age, we accumulate **senescent cells**, dysfunctional cells that refuse to die off. These cells are associated with accelerated aging and age-related disease.
- **Senolytics** are compounds that can *remove* senescent cells, helping to maintain optimal function and youthful health. In preclinical studies, senolytics slow or even reverse aging.
- The compound **fisetin** is one of the most potent plant-derived senolytics ever discovered. In animal research, it effectively removes senescent cells and boosts longevity. Old mice given fisetin had their lifespans extended by nearly **10%**.
- **Quercetin** is another plant compound that has significant senolytic effects and improves markers of health. It is even more powerful when enhanced with senolytic black tea compounds called **theaflavins**.
- **Fisetin**, **quercetin**, **theaflavins, and apigenin** are nutrients with senolytic activity.

The medical literature supporting the **senolytic** effects of quercetin has been growing over many years.[32,33,35,60,63-65]

In a study published in late 2019, quercetin successfully removed senescent cells in the kidneys of mice. This improved function and decreased the fibrosis (scarring) that leads to **kidney failure**.[49]

Quercetin can be difficult to absorb.[66] Scientists got around this problem by combining it with a type of fatty substance called a ***phospholipid***. The phospholipid serves as a **carrier**, allowing much more quercetin to enter the bloodstream and exert its effects throughout the body.[67]

Boosting Quercetin's Effects

Research has shown that quercetin works even *more effectively* when coupled with a chemotherapy drug, **dasatinib**.

When this combination was administered to old mice, its ability to eliminate senescent cells led to improvements in grip strength, coat condition, movement, and overall health.[32]

The first human study of this combination was published in 2019. Patients with **idiopathic pulmonary fibrosis** (a progressive lung disease) were given **100 mg/day** dasatinib and **1,250 mg/day** quercetin on three consecutive days per week for three weeks.[68]

This improved several measurements of **physical activity**, including distance walked and walking speed.

Scientists set out to identify a compound that would enhance quercetin's senolytic effects by the same mechanisms as dasatinib, but *without* the side effects of a cancer drug.[69-72]

The most effective candidate they found was a group of compounds in black tea called **theaflavins**.

In a similar way to dasatinib, **theaflavins** block an anti-apoptotic protein called **BCL-2**.[69,73] If you wonder what BCL stands for, it is "**B-cell lymphoma**."

A compound that blocks **BCL-2** might reduce risk of this common malignancy.

In a mouse study, **theaflavins** demonstrated significant **senolytic** effects.[73]

Targeting Toxic Secretions Emitted by Senescent Cells

Apigenin is a flavonoid found in certain herbs, fruits, and vegetables.

In two recent studies, **apigenin** was found to ***inhibit*** the **SASP**, also known as the senescence-associated secretory phenotype. This resulted in a reduction of **pro-inflammatory** compounds produced by senescent cells.[74,75]

Reducing **inflammation** caused by the **SASP** while diminishing the **senescent cell burden** gives a two-pronged strategy for fighting this enemy of longevity.

Quercetin and **theaflavins** (from black tea) function via separate and complementary mechanisms to purge the body of **senescent cells**.

Intermittent or Continual Therapy: Which Senolytic Program is Most Effective?

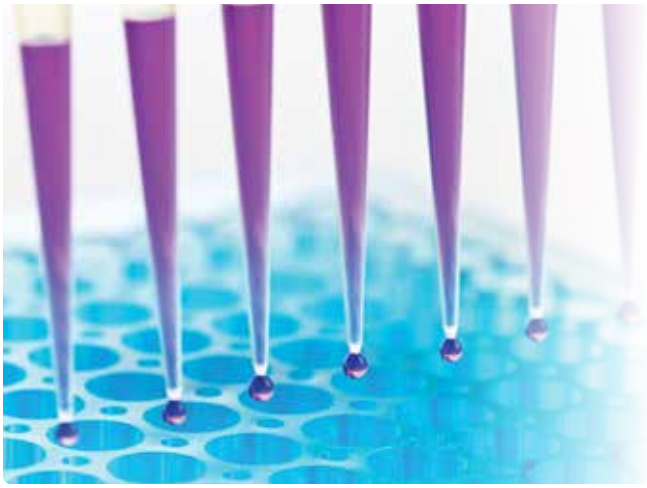
There's a great deal of debate in the longevity community about the ideal treatment regimen for **senolytic** therapies.

For now, **intermittent therapy** appears to be the best approach to reducing senescent cells.[32,33,64] Drugs that reduce expression of pro-inflammatory compounds secreted by senescent cells, for example, seem more effective when taken on an intermittent basis.[76]

Based upon the available preclinical research, **once-weekly** ingestion of high doses of **fisetin**, **quercetin**, **theaflavins,** and **apigenin** appears to be the optimal **senolytic** approach.

Fisetin, a strawberry flavonoid, has been shown to be the **most effective senolytic** when compared to a panel of flavonoids, removing aged, dysfunctional **senescent cells** in preclinical studies.

A multi-targeted approach utilizing highly absorbable **quercetin** and **fisetin**, plus **theaflavins**, and **apigenin,** can attack **cellular senescence** from multiple angles, helping to rid the body of the damage it causes.



Summary

Old or dysfunctional cells promote **chronic inflammation** and contribute to loss of function and increased risk for age-related disease.

Senolytics can cleanse the body of these cells, improving organ function and preventing disease.

A plant extract called **fisetin** has been identified as the most powerful senolytic known so far. An innovative formulation has enhanced fisetin's absorption up to **25 times**.

Fisetin by itself or combined with other known senolytic ingredients such as **quercetin and theaflavins,** may provide *superior* **senolytic** benefits. •

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- **APIGENIN** (a flavonoid)
- **BIO-FISETIN** (up to **25 times** greater bioavailability)

The suggested dose of the new **Senolytic Activator®** is **3 capsules** once a week. Each bottle lasts 3 months.

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What is **Tart Cherry**?

BY CHANCELLOR FALOON

Tart cherries, also known as sour cherries, contain compounds, including a class of **polyphenols** known as **anthocyanins**, that help reduce inflammation and oxidative stress.[1,2]

Research has shown that tart cherries can relieve arthritis pain, boost cognition, improve cardiovascular health, benefit endurance athletes, and target the underlying factors of gout.[1,3]

Tart cherries have been widely used to boost recovery and performance for athletes.

A **2020** meta-analysis of trials on endurance athletes confirmed that tart cherry concentrate intake significantly improves **endurance exercise performance**.[4]

In recent randomized controlled trials, those drinking **tart cherry** juice had improvements in a variety of areas:

- Healthy older adults who drank **two cups (16 oz)** of tart cherry juice daily for 12 weeks had improved scores on tests of **cognitive abilities**, including reaction time, a learning task, and spatial working memory compared to baseline.[5]
- In subjects 50 and older suffering from **insomnia**, drinking **one cup (8 oz)** of tart cherry juice twice daily for two weeks led to increased sleep time and sleep efficiency. Researchers noted that tart cherry juice prevented the degradation of **tryptophan**, an essential amino acid that may help treat sleep disorders.[6]
- In overweight or obese individuals, **one cup (8 oz)/day** of tart cherry juice reduced serum **uric acid concentration** by **19.2%** and **C-reactive protein** (a marker of inflammation) by **19.4%**.[7] Elevated blood uric acid is the underlying cause of gout, which is a painful form of arthritis.[8]

Tart cherries and their juice are naturally high in **sugar**. Many people prefer to avoid this sugar load and take **tart cherry extract** instead.

In one study, taking **tart cherry extract** was **15.4%** more effective at reducing the odds of a **gout attack** than eating cherries.[9]

A wealth of data shows that tart cherry extract can provide a wide range of health benefits.

A potential new use for tart cherry extract has been uncovered.

When components of tart cherry were tested on **oral** epithelial cells (cells that line the surfaces of the mouth), they improved the protective **barrier function**. Tart cherry also reduced the ability of oral pathogens to clump together in sticky white plaque that forms on teeth and gums.[10]

In a different study, tart cherry extract reduced growth and activity of the bacteria that are the main cause of **gingivitis** (inflammation of the gums).[11,12] These studies suggest that tart cherry extract fights oral pathogens and may help prevent and treat **oral plaque**. •

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We've combined black tea theaflavins and the plant-derived flavonoid apigenin with ultra-absorbable forms of the bioflavonoids quercetin and now fisetin to help manage senescent cell burden and promote systemic rejuvenation. This innovative, once-weekly formula is a powerful ally in our continuing fight to enhance longevity at the cellular level. (Now shipping in bottles instead of blister packs.)

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More energy, less stress. That's Ginseng Energy BOOST.

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Ginseng has been used to promote health for centuries. But to get the most out of its biologically active components, you need to use fermented ginseng extract. Doing so boosts absorption, so you get the healthy cellular energy pick-me-up you're looking for… no caffeine required. **Try Ginseng Energy Boost today.**

Maintain a balanced, healthy immune response

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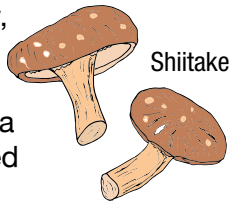
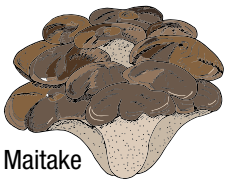


β-glucans (pronounced "beta glucans") are polysaccharides: soluble dietary fibers found in baker's yeast, mushrooms and oats. They help activate your immune system's primary defenders: macrophages, neutrophils and natural killer cells. Doing so helps your immune system to react faster and smarter when faced with challenges.



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