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# Vitamin D's: Winter Immune Benefits

**PLUS:** The Dangers of Overprescribing Statin Drugs



Item #02497  
60 Softgels

# Triple Protection for Your Ticker.

Your heart keeps the beat for your entire body. Hidden inside your arteries and veins is the vascular endothelium—a thin layer of cells that keeps your system running like clockwork.

**NEW Endothelial Defense™ Pomegranate Plus** keeps your cardiovascular gears turning with pomegranate, melon extract and more.

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

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

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

This product is available at fine health food stores everywhere.

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Climb

Jump

Swim

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**JUST TWO CAPSULES A DAY PROVIDE:**

Glucosamine sulfate 2KCl (derived from non-GMO corn)	1,500 mg
AprèsFlex <sup>®</sup> Indian frankincense ( <i>Boswellia serrata</i> ) extract (gum resin) [std. to 20% AKBA]	100 mg
NT2 Collagen <sup>™</sup> standardized cartilage	40 mg
Total Collagen	10 mg
Boron (calcium fructoborate as patented FruiteX-B <sup>®</sup> OsteoBoron <sup>®</sup> )	1.5 mg

Item #02238 • 60 capsules



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<sup>†</sup> 3-O-acetyl-II-ketoB-boswellic acid.

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Do you lack motivation? Well, it's time  
to get up off the mat and fight back!

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1. **Lutein, trans-zeaxanthin, and meso-zeaxanthin** to help maintain structural integrity of the **macula** and **retina**.<sup>1-5</sup>
2. **Alpha-carotene** to further help support **macular density**.<sup>1</sup>
3. **Cyanidin-3-glucoside** to assist with night vision.<sup>6-8</sup>
4. **Astaxanthin** for comprehensive eye health support and to fight eye fatigue.<sup>9</sup>
5. **Saffron** to help support vision, based on study subjects seeing an average of two additional lines on eye chart used by doctors to test vision.<sup>1</sup>



Item #01993 • 60 softgels

Each bottle lasts for two months.

## References

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

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Can't  
Compete**

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- 10 times the biotin
- 10 times the selenium
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- 2 times the vitamin D
- 2 times the vitamin E
- 2 times the zinc

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(Two-month supply)



### Two-Per-Day Tablets

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



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

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**VITAMIN D'S WINTER  
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**93** Onions provide sulfur and important **antiviral** and **immune-boosting** properties. Their compounds support heart health and bone density and may reduce the risk of certain cancers.



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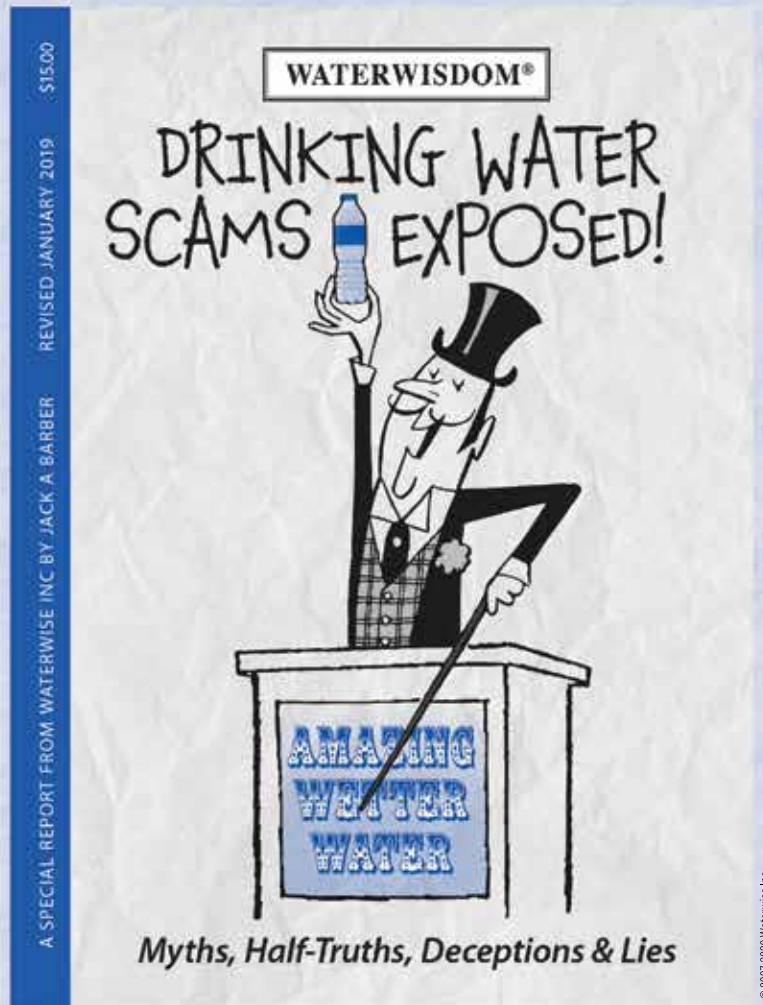
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Riboflavin (vitamin B2)	25 mg

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



This product is available at fine health food stores everywhere.

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# In the News



## Sleep is Important for the Immune System

Getting adequate sleep is important for well-being and health in many ways. Recently, a major international, interdisciplinary workshop sponsored by the *National Institutes of Health* highlighted the importance of sleep for regulating the immune system. A summary of the workshop was published in *JCI Insight*.\*

Lack of sleep has been associated with an increased vulnerability to infection, reduced antibody titers (a measurement of the level of antibodies in the blood) after vaccination, and reduced lifespan.

Sleep deprivation has been shown to reduce the efficacy of the flu vaccine. And animal studies have demonstrated that sleep is connected to the body's ability to resist infection.

Studies have revealed that sleep deprivation impairs the function of natural killer cells (part of the innate immune system). Lack of sleep also disrupts the circadian rhythm, which encourages inflammation and functional immunocompromise, making organisms more vulnerable to disease.

**Editor's Note:** The authors concluded that, "While connections to adaptive immunity and neuroinflammatory reflexes represent some highly opportune areas for study in the present, there are many areas of disease physiology for which the insights of circadian and sleep biology have yet to be considered."

\* *JCI Insight*. 2020 Jan 16; 5(1): e131487.

## Eating More Olive Oil May Lower Heart Disease Risk

Higher consumption of olive oil is associated with a lower risk of heart disease, according to a study published in the *Journal of the American College of Cardiology*.\*

The study included more than 61,000 women from the Nurse's Health Study and over 31,000 men from the Health Professionals Follow-up Study. Both studies lasted 24 years, and people completed food-frequency questionnaires at the beginning of the study, and every four years thereafter.

The results showed that people with a *higher* intake of olive oil had a **14%** lower risk of cardiovascular disease and an **18%** lower risk of coronary heart disease, compared to those who consumed less.

Higher intake was defined as greater than **0.5 tablespoons** (or greater than **7 grams**) per day. In addition, replacing just **5 grams** per day of margarine, butter, mayonnaise, or dairy fat, with an equivalent amount of olive oil, was associated with a **5%** lower risk of cardiovascular disease, and a **7%** lower risk of coronary heart disease.

**Editor's Note:** Potent antioxidant compounds called polyphenols contribute many of olive oil's beneficial effects.

\* *J Am Coll Cardiol*. 2020 Apr 21;75(15):1729-1739.



## Low Vitamin D Linked to Lower-Back Pain in Postmenopausal Women

A retrospective study reported in *Menopause*, the Journal of The North American Menopause Society, uncovered an association between deficient levels of vitamin D and disc degeneration, with resulting lower-back pain, in postmenopausal women.\*

Researchers evaluated data concerning lumbar disc degeneration, serum 25-hydroxyvitamin D levels, and markers of bone turnover in 232 postmenopausal women.

Vitamin D levels of more than **30 ng/mL**, categorized as normal, were present in **12.5%** of the subjects, and severely deficient levels of less than **10 ng/mL** were found in **12.9%**.

Women who were severely deficient in vitamin D had higher scores for low-back pain and lower bone-mineral-density scores than the remainder of the participants. Decreased vitamin D levels were associated with increasing severity of disc degeneration.

**Editor's Note:** "Smoking, severe vitamin D deficiency, lack of vitamin D supplementation, high body-mass index, and osteoporosis are associated with a higher prevalence of moderate to severe pain," the authors concluded.

\* *Menopause*. 2020 May;27(5):586-592.



## Adding Spices to Meals May Benefit Health

A recent study published in *The Journal of Nutrition* suggests that people may be able to lower post-meal inflammation by spicing up the food.\*

In a crossover study, overweight men with risk factors for cardiovascular disease were provided with a high-fat, high-carbohydrate meal, with or without the addition of **two grams** or **six grams** of a mixture of basil, bay leaf, black pepper, cinnamon, coriander, cumin, ginger, oregano, parsley, red pepper, rosemary, thyme and turmeric. The experiment was repeated on two following days in which the administration of the meal/spice combinations were rotated among the participants to enable each to receive all three combinations during the study.

Blood samples collected prior to and hourly for four hours after the meal were analyzed for factors relating to inflammation. Four hours after consumption, the meal that contained **six grams** of the spices was associated with a reduction in the secretion of a proinflammatory cytokine known as interleukin-1beta.

**Editor's Note:** Postprandial proinflammatory cytokine secretion, which describes the increase in inflammatory factors that occurs after consuming a high-fat or high-carbohydrate meal, is associated with an elevated risk of cardiovascular disease.

\* *J Nutr*. 2020 Jun 1;150(6):1600-9.

## Glucosamine Supplementation Linked to Lower Mortality Risk

There was a lower risk of death from cardiovascular disease, cancer, respiratory disease, digestive diseases, or any cause, among individuals who supplemented with **glucosamine**, in comparison with those who didn't, a study published in *Annals of the Rheumatic Diseases* found.\*

Researchers looked at 495,077 participants enrolled in the UK Biobank study. During a median of 8.9 years, 19,882 deaths occurred, which included 3,802 deaths from cardiovascular disease, 8,090 from cancer, 3,380 from respiratory disease and 1,061 from digestive disease.

Regular use of glucosamine supplements was reported by **19.1%** of the participants at baseline.

Those individuals who regularly supplemented with glucosamine, compared to those who didn't, had:

- **27%** lower risk of death from respiratory disease,
- **26%** lower risk of dying from digestive disease,
- **18%** lower risk of death from cardiovascular disease,
- **6%** lower risk of dying from cancer, and
- **15%** lower risk of death from any cause.

**Editor's Note:** Glucosamine is a nutritional supplement used in the management of arthritis and joint pain. These newly identified benefits are being studied now to ascertain if supplementing with **500-1500 mg** a day of **glucosamine** might be an effective way to reduce the risk of age-related disorders and all-cause mortality.

\* *Ann Rheum Dis.* 2020 Jun;79(6):829-836.



## Eating Less Salt Helps Support Healthy Immune Function

One simple way to help maintain healthy immune function is to lower salt intake, according to a study published in *Science Translational Medicine*.\*

Researchers studied the effects of a high-salt diet in mice and humans. Mice infected with listeria that received a high-salt diet had 100 to 1,000 times more of the bacteria in their spleens and livers than animals that consumed normal diets.

In humans who consumed an extra **six grams** of salt per day, immune cells in the blood known as granulocytes were less effective against bacteria, and levels of glucocorticoids increased.

When a high amount of salt is consumed, it is filtered by the kidneys, whose sodium chloride sensor activates salt excretion in the urine. This sensor is also responsible for the accumulation of glucocorticoids that inhibit the function of granulocytes that primarily attack bacteria. When granulocyte function is impaired, infections are more severe.

**Editor's Note:** Additionally, according to the World Health Organization, "Salt intake of less than **five grams** per day for adults helps to reduce blood pressure and risk of cardiovascular disease, stroke, and coronary heart attack."

\* *Sci Transl Med.* 2020 Mar 25;12(536).

## Metformin Use Associated with Improved Postoperative Survival Among Diabetics

A lower risk of readmission or mortality following surgery was found among patients who were using the antidiabetic prescription medication metformin, research reported in *JAMA Surgery* revealed.\*

The study included 10,088 diabetics who were hospitalized for major surgery between January 2010 and January 2016. There were 5,962 individuals who had a prescription for metformin during 180 days prior to their surgery, who were matched with 5,460 people who did not have a prescription.

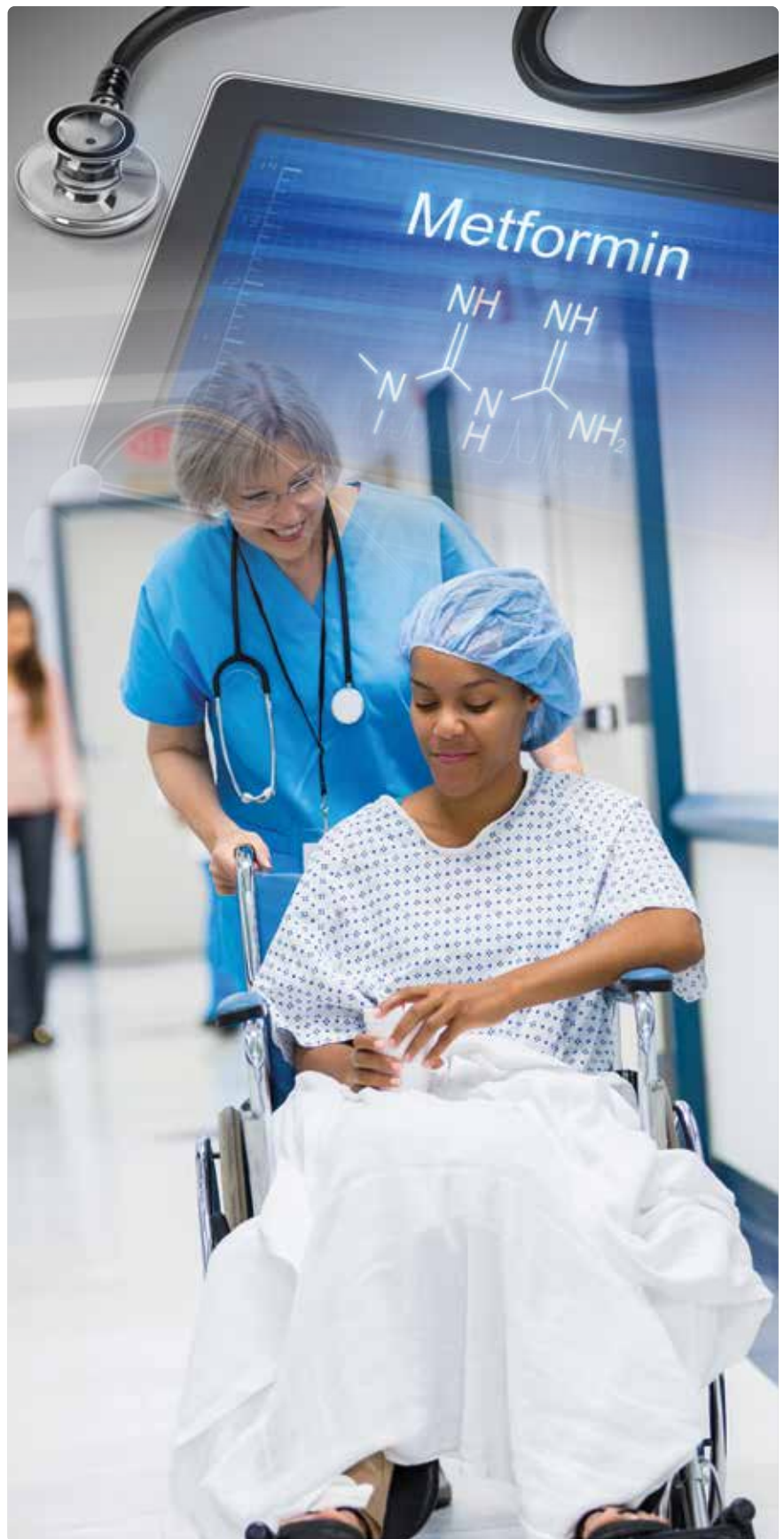
Having a prescription for metformin was associated with a **28%** lower 90-day postoperative mortality risk compared to the risk experienced by those who were not using the drug.

Metformin was also associated with a lower 30-day and 90-day postoperative risk of readmission, indicating fewer postoperative complications.

It was further determined that metformin was associated with a **22%** increase in five-year survival in comparison with not having been prescribed the drug.

**Editor's Note:** Preoperative inflammation, as determined by the ratio of white blood cells known as neutrophils to leukocytes, was significantly lower among metformin-treated patients, which may be one mechanism through which the drug confers its protective effects.

\* *JAMA Surg.* 2020 Apr 8;155(6):e200416.







## Reduced Heart Failure with Higher Magnesium Intake

Research findings published in the *Journal of the American Heart Association* show a lower risk of heart failure among participants in the Women's Health Initiative (WHI) who had a greater intake of magnesium, compared to those whose intake was low.\*

The study evaluated data from 97,725 postmenopausal women who were free of heart failure on enrollment. Questionnaires completed by the participants after enrolling were evaluated for magnesium intake from food and supplements. During a median follow-up period of 8.1 years, 2,153 hospitalizations for heart failure occurred.

Compared to the top **25%** of magnesium consumers, who ingested an average of **461 mg** per day, women whose intake was among the lowest **25%** at **207.5 mg** per day had a **26%** greater adjusted risk of heart failure.

When magnesium from food alone was analyzed, the risk of heart failure for those consuming the least amount was **32%** higher than the group with the greatest consumption.

**Editor's Note:** "Women represent a large proportion of the growing heart failure epidemic, yet data are lacking regarding optimal dietary and lifestyle prevention strategies for them," the authors stated.

\* *J Am Heart Assoc.* 2020 Apr 7;9(7):e013570.

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# Are You *Resolving* INFLAMMATION?

BY CHANCELLOR FALOON

**Chronic inflammation** is connected to degenerative aging.

This has prompted scientists to coin the term “**inflammaging**” to describe this destructive process.<sup>1</sup>

Recent discoveries shed light on our understanding of **inflammaging**.<sup>2</sup>

Research shows that **resolution** of inflammation may be as important as **inhibition** of inflammation in the fight against age-related disorders.

The field of **inflammation resolution** is generating increasing interest.

This led scientists to identify compounds that help **resolve** inflammation. They are named:

## **Specialized pro-resolving mediators (SPMs)**

Increasing **SPM levels** in preclinical models yields compelling findings.<sup>3</sup>

Clinical trials are currently recruiting participants and publishing results.<sup>4</sup>

## How SPMs Resolve Inflammation

**Specialized pro-resolving mediators** are extracted from polyunsaturated fatty acids, predominantly found in **fish**.<sup>3</sup>

In response to certain conditions, such as **inflammation**, small amounts of omega-3 fatty acids are converted to even more beneficial compounds: **SPMs**.<sup>3</sup>

Chronic inflammatory conditions such as **inflammaging**, have been associated with lower concentrations of SPMs in the body.<sup>5</sup>

**SPMs** resolve inflammation by **three mechanisms**:<sup>6-8</sup>

- *Removing* dead and dying cells through a process in which **macrophage** immune cells engulf and digest dying or dead cells. This helps clean up the aftermath of inflammatory cascades.
- *Restoring* inflammation balance by decreasing **pro-inflammatory** mediators, while increasing compounds that have **anti-inflammatory** activity.
- *Renewing* damaged tissue by promoting cellular **regeneration**.

These benefits promise to help prevent many chronic aging disorders including deposition of plaque in the arteries (**atherosclerosis**).<sup>9</sup>

## Inflamed Arteries

Inflammation is a key player in the development of heart disease.

Atherosclerosis is partially driven by an *imbalance* between pro-inflammatory and **inflammation-resolving** mechanisms in the artery inner walls.<sup>9</sup>

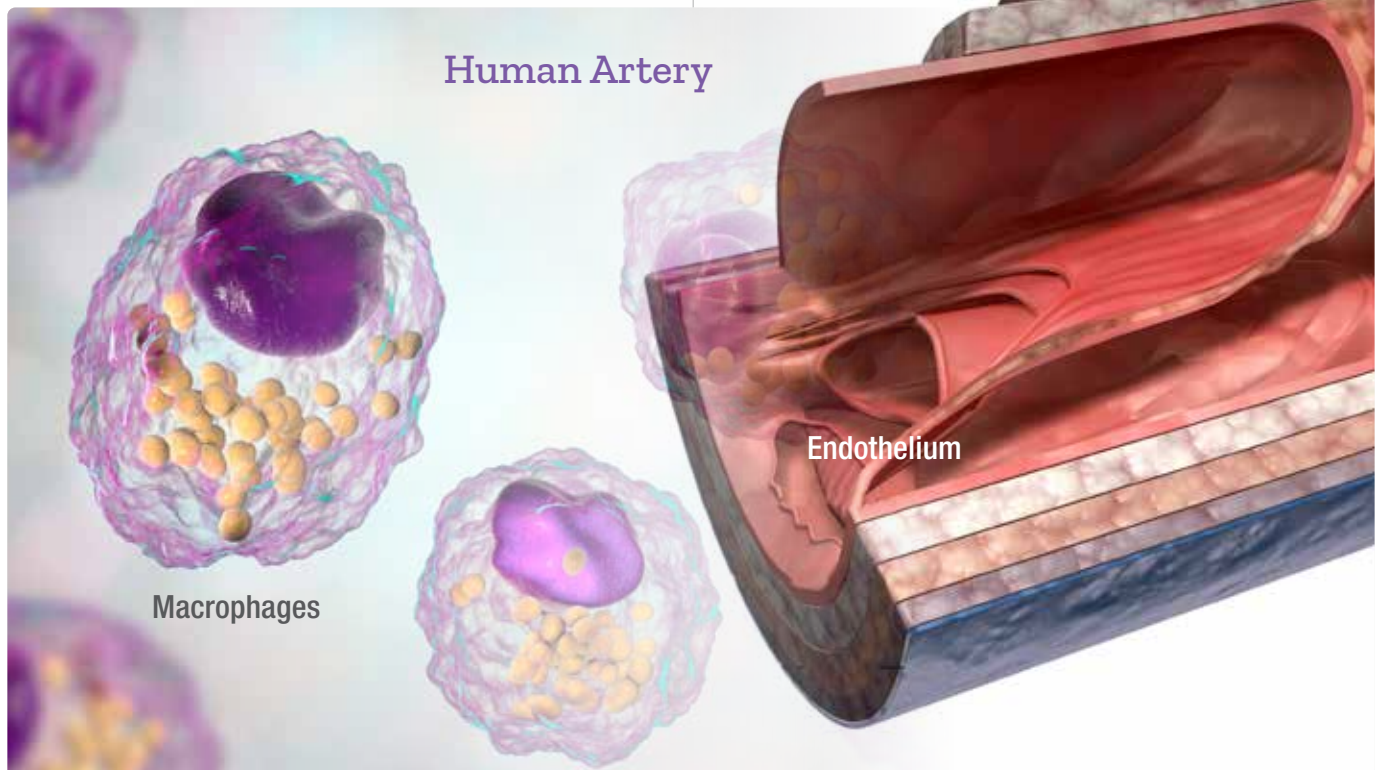
Atherosclerosis can begin when **LDL cholesterol** (the “bad” cholesterol) particles get trapped inside the endothelium (lining of the arteries).

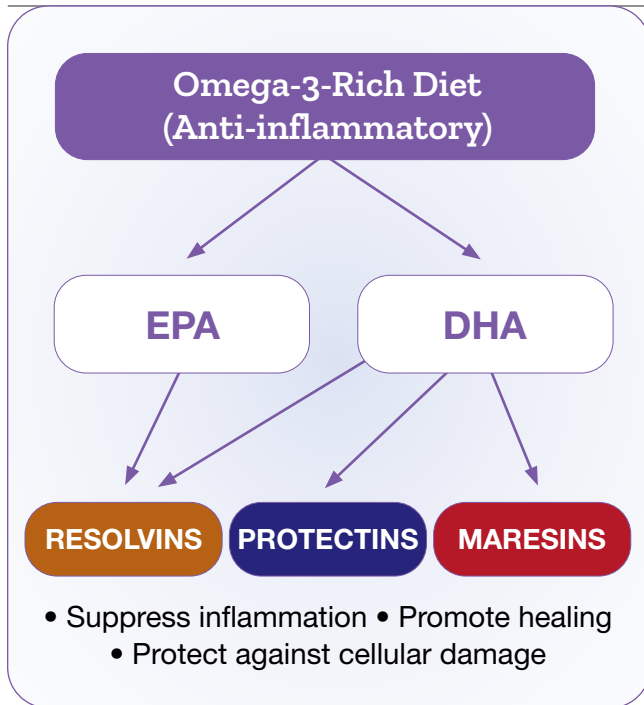
**Macrophages** enter the **endothelium** to clear out these oxidized LDL particles. If there is a lack of **pro-resolving mediators**, these macrophages will change into **foam cells**.<sup>9</sup>

This is a dangerous state that generally results in the **foam cells** dying and releasing their contents, creating an even *greater* **pro-inflammatory** environment.<sup>9</sup>

SPMs come into play here by initiating the *removal* of dead cells and foam cells through a process called **efferocytosis**.

If these cells are *not* removed, they contribute to plaque progression, which leads to atherosclerosis that endangers the heart, kidneys, and brain.<sup>9,10</sup>





### How SPMs Differ from Omega-3s

The process of converting omega-3 fatty acids into SPMs requires several steps in the body.

When one eats cold water fish or takes fish oil supplements, tiny amounts may be converted to **pro-resolving mediators** (SPMs).

To meaningfully resolve **inflammaging**, *higher* amounts of standardized **SPMs** are often required beyond what can be obtained with fish oil.

### Preclinical Research on SPM Precursors

In preclinical studies, SPMs *and* SPM precursors have been shown to have a variety of biological benefits.

A clinical trial of a combination of omega-3 fatty acids and SPMs demonstrates powerful effects on a range of immune, inflammatory, and blood-clotting indices.

Studies in mice have demonstrated impressive **resolution** benefits in a variety of disease models using the SPM precursor **18-HEPE**.

**SPM precursors** enable formation of **specialized pro-resolving mediators** (SPMs) in the body.

One study involved a rodent model that mimics some of the complications related to **cardiovascular disease**. Following surgery, researchers injected mice with the SPM precursor **18-HEPE** every three days.<sup>12</sup>

The mice that received **18-HEPE** were significantly shielded from damaging complications brought on by the surgical procedure.

Another study used a mouse model of **melanoma** metastasis. Researchers pretreated mouse **melanoma** cells with the SPM precursor **18-HEPE** while controls were not treated.

Healthy mice were then administered the SPM precursor 18-HEPE-treated **melanoma** cells *and* received additional 18-HEPE injections every other day. The SPM precursor-treated mice had significantly *less* formation of tumor colonies compared to controls.<sup>13</sup>

Another group of researchers found that treatment with the SPM precursor **17-HDHA** was able to *reverse* pain behavior in two rat models of osteoarthritis.<sup>14</sup>

### The Science Behind Specialized Pro-Resolving Mediators (SPMs)

SPM *precursors* are predominantly derived from the **omega-3** fatty acids EPA and DHA.

But obtaining meaningful **potencies** of **SPMs** requires a series of complex metabolic processes that are often lacking in aging individuals.

The omega-3 fatty acid **precursors** needed to produce SPMs in the body include:<sup>11</sup>

- **18-HEPE**  
(18-hydroxyeicosapentaenoic acid)
- **17-HDHA**  
(17-hydroxydocosahexaenoic acid)
- **14-HDHA**  
(14-hydroxydocosahexaenoic acid).

These **precursors** listed above are then **converted** into the following **specialized pro-resolving mediators** (SPMs):

- **Resolvins**
- **Protectins**
- **Maresins**

These make up the bulk of the SPMs that target inflammation through the three steps of **removing, restoring and renewing**.

## New Human Trial of SPM Precursors

A human trial of SPM precursors was published in **January 2020** and showed remarkable results.

In this study, 22 healthy volunteers aged 19 to 37 were randomized. One group received an enriched fish oil supplement containing omega-3 PUFAs *plus* a combination of SPM precursors, including **18-HEPE**, **17-HDHA**, and **14-HDHA**. The other group received a **placebo**.<sup>18</sup>

Researchers separated the participants into different dosing groups and performed a series of tests. They were able to conclude that the **SPM precursors**:

- Significantly increased cell surface proteins involved in **reversing inflammation** and **platelet aggregation** (which leads to harmful clotting) caused by the addition of a pro-inflammatory stimulus in the drawn blood of the patients.
- Increased clearance of *Staphylococcus aureus* and *E. coli*, by immune cells, which was highest at the final measurement, after 24 hours.
- Decreased **platelet activation**, a central part of the process that leads to a blood clot, in association with an increased level of **resolvins**.
- Increased the expression of genes linked to immune responses, recruitment of immune cells that fight infection and other diseases, and cellular metabolism in peripheral blood cells.

## Omega-3s Help Resolve Inflammation

Because the original sources of SPMs are primarily the **omega-3 fatty acids** EPA and DHA, increasing the intake of these healthy fats will assist in resolving inflammation.<sup>19-21</sup>

In a recent clinical trial, researchers showed that in response to a pro-inflammatory stimulus, **EPA** and **DHA** intake leads to the formation of more SPMs.<sup>21</sup>

For five months, participants were given either EPA and DHA or a placebo daily, before receiving a **pro-inflammatory stimulus**. Blood was collected daily for five days after receiving the stimulus.

By the fifth day, the group that received the EPA and DHA had **229% higher** SPM levels than the placebo group. The levels of systemic inflammation, as measured by **C-reactive protein**, were significantly lower in the EPA/DHA treatment group compared to placebo.

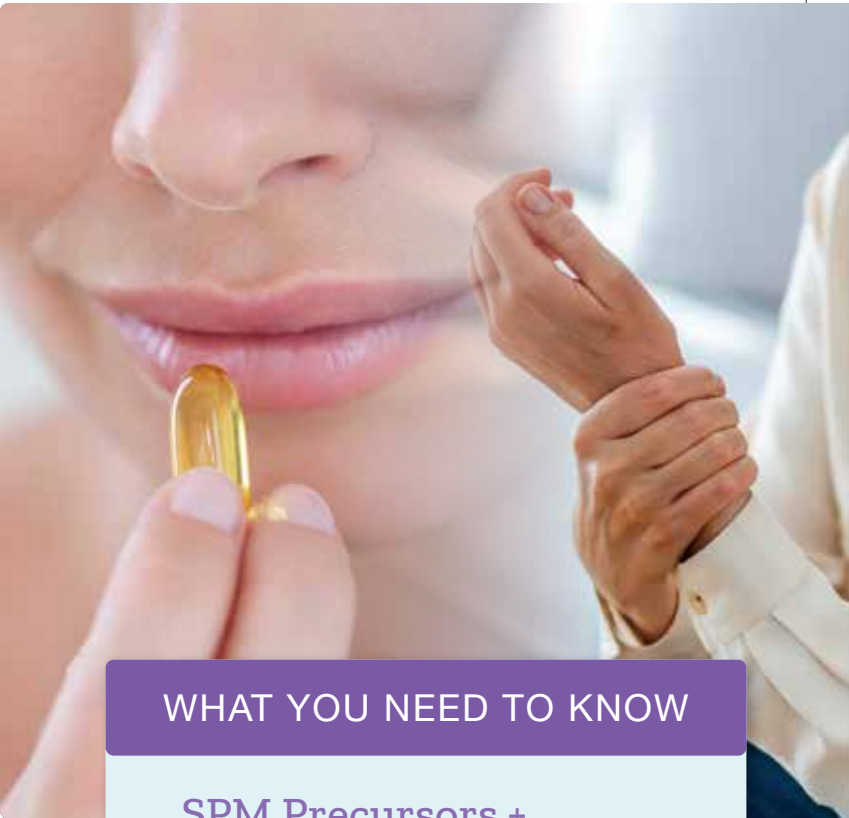
The researchers repeated this testing using slight variations with their methods. Results consistently showed that EPA and DHA intake *increases* the level of SPMs in response to a pro-inflammatory stimulus.

This is great news for those who eat lots of **cold-water fish** and/or take high-potency **fish oil** supplements. Those with potential **inflammaging** issues may want to add a supplement providing **standardized** potencies of:

- **Resolvins**
- **Protectins**
- **Maresins**







## WHAT YOU NEED TO KNOW

### SPM Precursors + Omega-3s Resolve Inflammation

- **Chronic inflammation** is a major risk factor in aging, age-related disease, and degenerative disorders.
- Scientists have identified compounds that *resolve* inflammation, called **specialized pro-resolving mediators (SPMs)**.
- SPMs are mostly derived from the **omega-3 fatty acids** EPA and DHA, which are primarily found in fish. A recent clinical trial showed that supplementation with a marine oil enriched with SPM precursors increases SPM levels and helps resolve inflammation.
- Another clinical trial showed that supplementation with omega-3s also increased SPMs in the body and helped lower levels of the inflammatory marker C-reactive protein.

### Preclinical Research on SPMs

Preclinical data demonstrate promising results from the *direct* use of **specialized pro-resolving mediators (SPMs)**.

In one study, researchers tested the effects of an **SPM resolvin** on mice that had obesity-associated **osteoarthritis**. The treatment was injected into the animals' joints. The results showed a significant *reduction* in pro-inflammatory macrophage infiltration into the soft tissue surrounding the joints (**synovium**), reduced severity of synovium inflammation, and prevention of cartilage degradation.<sup>15</sup>

A review of preclinical studies concluded that SPMs may be an effective treatment for gum disease (**periodontitis**). These studies showed that topical application of a **resolvin** and a **lipoxin** (an omega-6-derived SPM) to inflamed periodontal tissue results in a significant prevention of tooth loss compared to the control group.<sup>16</sup>

A mouse study showed that injections with the SPM **maresin** reduced inflammation-induced **neuropathic pain**.<sup>17</sup>

### Summary

Chronic inflammation is so strongly correlated with age that scientists describe it as **inflammaging**.<sup>1</sup>

For decades, researchers have been studying how to better inhibit inflammation. They are now also beginning to understand the importance of **resolving** inflammation.

An abundance of preclinical data has demonstrated substantial potential benefits of having higher levels of **specialized pro-resolving mediators (SPMs)** or SPM precursors.

Polyunsaturated fatty acids, particularly the **omega-3** class, can be made into **SPMs** in your body. However, taking **SPM precursors** directly may be more effective.

Those concerned about chronic inflammation and persistently elevated inflammatory markers (like C-reactive protein and interleukin-6) may want to add a **multi-SPM** formula to their intake of omega-3 fatty acids.

Several clinical trials on SPM precursors are underway, with some completed and some still recruiting participants.<sup>4</sup>

**Life Extension®** is also now recruiting generally healthy people for a clinical trial. If you are in the Fort Lauderdale area and are interested in participating, please call **1-866-517-4536**.

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## Weight Loss Increases SPMs

In a recent study, researchers discovered that **weight loss** leads to a significant *increase* in the formation of **SPMs**.<sup>22</sup>

The researchers selected 42 patients with **metabolic syndrome** and took blood samples of their **neutrophils**, which are a short-lived type of white blood cell that eliminates pathogens.<sup>23</sup> The researchers then stimulated the neutrophils and measured the release of SPMs to use for comparison after the intervention.

Patients were randomly selected to go through either a **weight loss** program (treatment) or a **weight stabilization** program (control).

After 16 weeks, the researchers again took blood samples of their neutrophils and provided stimulation to measure the amount of SPM release.

At the end of the trial, the SPM release from the neutrophils of the patients in the **control group** was **unchanged** compared to baseline.

The **weight loss group** had significantly *elevated* SPM release compared to baseline. Compared to the control group, weight loss led to a **2-fold** increase the release of the SPM **E-series resolvin**.

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The background of the page is a dense field of yellow, oval-shaped capsules, likely representing vitamin D supplements. On the left side, there is a vertical strip showing a close-up of a blue and orange virus particle, possibly a coronavirus, with its characteristic spike proteins.

# VITAMIN D'S

## Winter Immune Benefits

BY JULIE MYERS

**Vitamin D** has shown promise against winter illness because it plays a critical role in supporting the **immune system**.

*Low* vitamin D levels have been associated with *higher* rates of many chronic diseases.<sup>1-6</sup>

This includes an *increased* risk for acute communicable diseases, including **viral infections** in **vitamin D deficient** people.<sup>7,8</sup>

A meta-analysis of randomized, controlled clinical trials showed a protective effect against **acute respiratory infections** with vitamin D supplementation.<sup>9</sup>

More than **40%** of Americans have been found to have **insufficient** blood levels of vitamin D (defined as levels between **20-30 ng/mL**).

An additional nearly **30%** of Americans have lower vitamin D levels (**below 20 ng/mL**) that qualify as **deficiency**.<sup>10</sup>

This factor may be especially important among adults aged 60 and over.<sup>10</sup>

**Life Extension®** supporters have long been advised of the importance of maintaining an optimal vitamin D level between **50-80 ng/mL**.

Oral intake of **vitamin D** to ensure healthy levels may help protect against winter-season conditions.

### Impact on Immune Function

For the body to produce its own **vitamin D**, we need direct skin exposure to sunlight.

But we spend most of our time indoors or covered up by clothes and sunscreen. And spending more time in the sun raises the risk of skin cancer and accelerated skin aging.

The other way to get vitamin D is through diet, but most foods contain only modest amounts.

As a result, a majority of people are getting too little of this crucial vitamin.

Having low levels of vitamin D is associated with a greater risk for many health problems, from cognitive decline to heart disease.<sup>1-6</sup>

Vitamin D supports **immune health** by helping:<sup>7,8</sup>

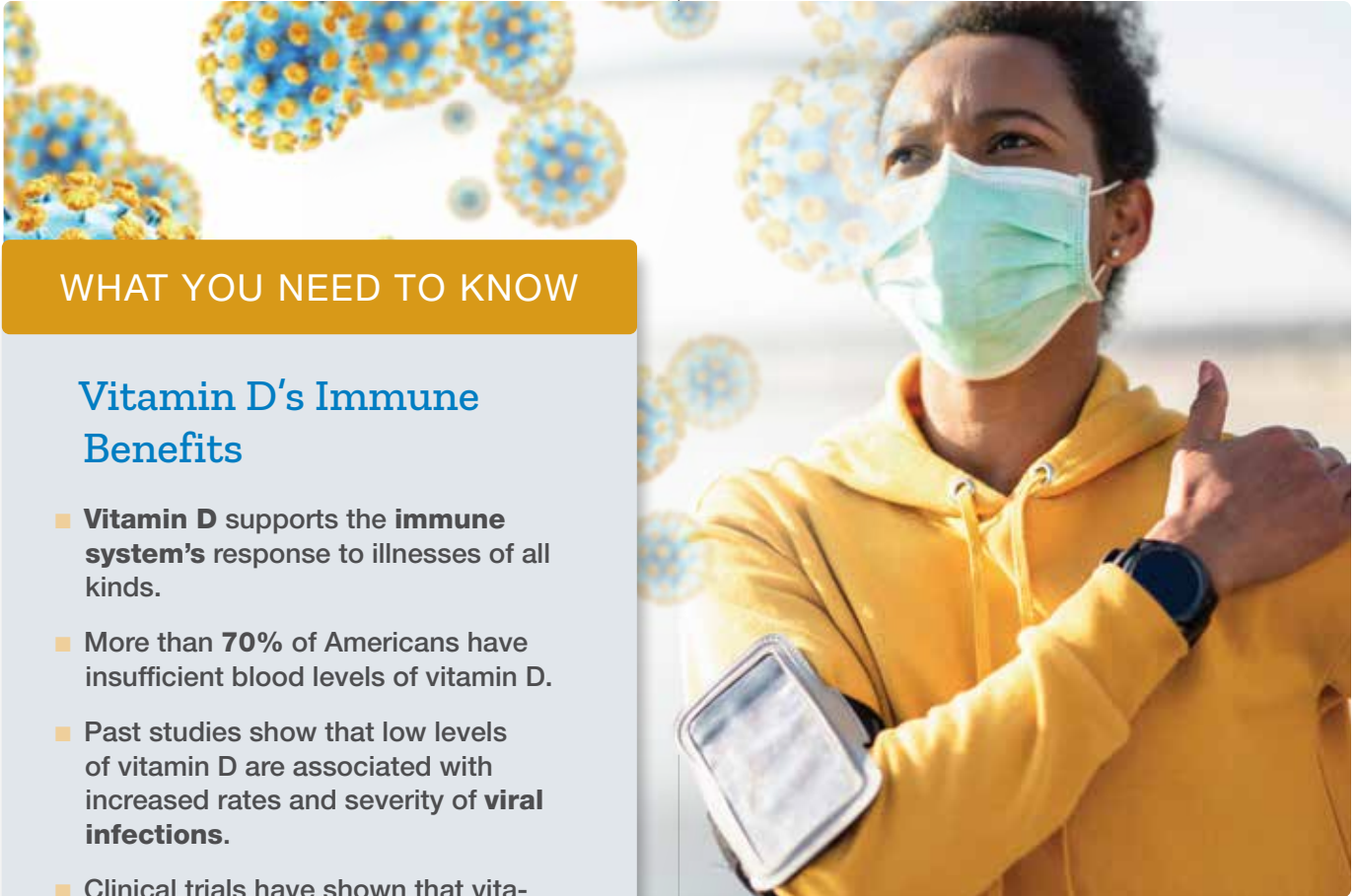
- Optimize immune function that protects us from infectious disease.
- Control *overly* aggressive inflammatory immune responses, which can inflict systemic damage.

When excessive levels of immune-system proteins called **cytokines** provoke attacks on healthy tissues, the result is called a “**cytokine storm**.”

This is a dangerous reaction that can lead to **acute respiratory distress syndrome (ARDS)**, an often-fatal complication in which fluid collects in the lungs.







## WHAT YOU NEED TO KNOW

### Vitamin D's Immune Benefits

- **Vitamin D** supports the **immune system's** response to illnesses of all kinds.
- More than **70%** of Americans have insufficient blood levels of vitamin D.
- Past studies show that low levels of vitamin D are associated with increased rates and severity of **viral infections**.
- Clinical trials have shown that vitamin D has a protective effect against **respiratory tract infections**.

#### Vitamin D and Viral Illness

**Viral respiratory tract infections**, such as the flu, are more common during winter.

One of the reasons for this may be **seasonal variations** in our vitamin D levels. During winter, we get less sun, leading to lower vitamin D production.<sup>11,12</sup> That puts us at increased risk for viral infection.

Research shows that infections are *more* common and more severe in those with vitamin D *deficiency*.<sup>12,13</sup>

Low vitamin D is also a risk factor for more severe lung disease, including acute respiratory distress syndrome (**ARDS**).<sup>14,15</sup> Research suggests that those with insufficient vitamin D are at increased risk of a **cytokine storm**.<sup>16</sup>

This hyperproduction of inflammatory factors leads to worsening disease severity and increased risk of death. Low vitamin D levels may be associated with the dangerous inflammation that occurs in ARDS.<sup>14,15</sup>

#### Vitamin D's Protective Actions

Vitamin D contributes to many functions that help shield the body from infections and lessen their severity. Maintaining adequate levels of **vitamin D**:<sup>14,17-20</sup>

- Interferes with the ability of viruses to **replicate** and produce *more* viruses,
- Helps support and repair healthy cellular linings in the body, including in the airways of the **lungs**,
- Increases production of proteins that shield against **bacteria and viruses**, enhancing the ability of cells to protect themselves from infection,
- Improves the ability of **immune cells** to mount an effective attack against specific viruses, and
- Helps prevent the immune system from going overboard and producing *excessive* pro-inflammatory compounds in the lungs.

## Oral Vitamin D Reduces Risk

Many studies have evaluated whether daily **oral intake** of vitamin D can reduce rates of **viral respiratory illness**.

Meta-analyses of clinical trials have shown that vitamin D has a protective effect against **respiratory tract infections**.<sup>9,21</sup>

The impact of vitamin D treatment is greatest in those who, to begin with, have *low* levels of vitamin D.<sup>9</sup>

**Life Extension**® supporters have long been advised of the importance of maintaining an optimal vitamin D level between **50-80 ng/mL**, and yearly blood testing.

### Summary

**Vitamin D** supports the **immune system** in many different ways, helping to shield the respiratory tract from **viral illness**.

A large majority of adults have vitamin D levels below the optimal level.

Trials have shown that **oral vitamin D** intake modestly *decreases* rates of **viral respiratory tract infections**.•

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### Blood Testing Vitamin D Levels

There are no universal guidelines for frequency of vitamin D testing. However, given the high prevalence of vitamin D deficiency and the strong association of low vitamin D levels with several health issues, annual testing and supplementation to achieve adequate blood levels is highly recommended.

Annual blood tests can let people know whether they are taking the correct dosage to ensure optimal blood levels of vitamin D.

If you do not already maintain an optimal blood level of *25-hydroxyvitamin D* of **50 to 80 ng/mL**, then take between **5,000 to 8,000 IU** of vitamin D daily with meals.

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- Support strong bones<sup>5</sup>
- Maintain healthy cholesterol levels already within normal range<sup>6</sup>

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#### Mega Green Tea Extract Decaffeinated

Item #00954

100 vegetarian capsules

#### Mega Green Tea Extract Lightly Caffeinated

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

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



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



# BEYOND CBD: Plant-Based Endocannabinoid Support

BY PAUL JOHNSON

Scientists have discovered that the **endocannabinoid system** influences the balance and function of almost **all** bodily systems.

The endocannabinoid system plays an important role in **brain function**, influencing mood, learning and memory, pain control, sleep, appetite, and more.

But as we age, the endocannabinoid system becomes less active.<sup>1,2</sup> That can lead to accelerated aging and increased susceptibility to disease.<sup>1</sup>

Research has shown that the endocannabinoid system plays a profound role throughout the rest of the body, affecting everything from bone strength to fat and glucose metabolism.<sup>2</sup>

In the past years CBD (cannabidiol) products have become increasingly popular, ranging from a variety of formulations from oils to cosmetics.

This comes from the fact that CBD interacts with and supports the endocannabinoid system.

The problem is that there are many unanswered questions about the quality and efficacy of the CBD-containing products purchased commercially.

For those who want to improve their internal endocannabinoid functions, scientists have identified **four plant compounds** that favorably influence the endocannabinoid system in **multiple ways**.





### What Is the Endocannabinoid System?

Like hormones and nerve cells, the endocannabinoid system is a **cellular communication system**, allowing various cells to send *signals* to others.

It helps to regulate and maintain the optimal function of many bodily systems.

It also helps maintain **homeostasis**, stability in response to changes in the environment, throughout the body.

The endocannabinoid system is active in most tissues. It has been identified in brain, bone, muscle, liver, and fat tissue, immune cells, and more.<sup>1-3</sup>

It's made up of three parts:

- Signaling molecules called **endocannabinoids**,
- **Receptors** found throughout the body, to which the endocannabinoids bind to transmit a signal, and
- **Enzymes** which break down the endocannabinoids once their work is done.

Two of the best-known endocannabinoids are **anandamide (AEA)** and **2-arachidonoyl glycerol (2-AG)**. They interact with receptors throughout the body.

The name “endocannabinoid” comes from the fact that plant-based **cannabinoid** compounds, such

as those found in cannabis, influence **cannabinoid** receptors on cell membranes. “**Endo**” refers to something formed *within* the body.

Unlike cannabinoids from cannabis, **endocannabinoids** do *not* have psychoactive effects. But they have a profound impact on the brain and body.

### The Endocannabinoid System and the Brain

In the brain, the endocannabinoid system has been shown to be **neuroprotective**,<sup>1</sup> shielding brain cells against damage and age-related changes.

As a result, it is a promising research target in the battle to help protect against cognitive decline and diseases such as Alzheimer’s and Parkinson’s disease.<sup>1</sup>

Its effects in the brain also relate to many essential quality-of-life factors: mood, pain perception, cognition and memory, appetite regulation, and sleep.<sup>2,4</sup>

On a cellular level, scientists have found that the endocannabinoid system protects the brain by:<sup>1</sup>

- **Regulating brain “helper” cells.** The **glial cells** in the brain are support cells that are vital to normal brain function. The endocannabinoid system maintains their function, supporting brain cells, preventing inflammation, and guarding against neurodegeneration.



- **Promoting formation of new neurons.**

As we age, our ability to form new nerve cells declines. This is a major contributor to cognitive and functional decline. The endocannabinoid system *increases* neurogenesis, helping to maintain learning and memory.

- **Boosting synaptic plasticity.** The ability of our synapses, where neurons communicate, to adapt to new information also diminishes in old age. By strengthening this ability, known as synaptic plasticity, the endocannabinoid system can help prevent cognitive decline.

- **Increasing brain-derived neurotrophic factor.**

This protein supports the survival, growth, and health of neurons, which helps prevent neurological diseases, including Parkinson's and Alzheimer's.

## Body-Wide Effects

Beyond the brain, the endocannabinoid system has a wide range of effects. It has been found to regulate: <sup>2</sup>

- Bone remodeling, in which old bone tissue is replaced by strong, new bone,
- Gastrointestinal function,
- Fat metabolism in both the liver and in fatty tissues,
- Muscle metabolism, and
- Immune cell function.

## WHAT YOU NEED TO KNOW

### Strengthening the Endocannabinoid System

- The endocannabinoid system is a signaling system that operates throughout the body, from brain to bone.
- It helps regulate and bring balance to a wide range of bodily functions, which can slow the aging process and reduce risk for chronic disease.
- Researchers have discovered four compounds that influence endocannabinoid system function: **oleoylethanolamide (OEA)**, **biochanin A**, **guineensine**, and **beta-caryophyllene**.



## How the Endocannabinoid System Works

After discovering how diverse the effects of the endocannabinoid system are, scientists investigated *how* it works. They found that it contributes to all of the following:<sup>1</sup>

- **Cellular “housekeeping.”** Cannabinoids induce **autophagy**, when cells clear away damaged proteins and other compounds to make room for new, healthy cellular components.
- **Regulation and protection of mitochondria.** Mitochondria are the “powerhouses” of the cells. The endocannabinoid system helps regulate their normal activity and protect them from damage.
- **Modulating signaling and communication pathways.** Cell-to-cell interactions throughout the body rely in part on endocannabinoid signaling. These relationships have diverse effects, including impacts on sleep-wake cycles, pain perception, mood, learning, and memory.

All of these pathways are critical in slowing the aging process and maintaining normal tissue function in various organs.

## Supporting Endocannabinoid Function

Scientists have discovered that there are ways to influence the function of the endocannabinoid system—*without* resorting to use of **CBD** (cannabidiol), **THC** (tetrahydrocannabinol), or other potentially psychoactive cannabinoids from cannabis.

The following compounds have been found to influence the activity of the **endocannabinoid system** through distinct but complementary effects.

### Oleylethanolamide (OEA)

**Oleylethanolamide** is a fatty acid that is naturally produced in the body.

It is similar in structure to one of the endocannabinoid compounds.

**Oleylethanolamide’s** (OEA) activity to suppress inflammation and regulate metabolism and appetite is mediated through the activity of **endocannabinoid** receptors but without binding to them.<sup>5-7</sup>

OEA has also been found to have neuroprotective effects and to provide support against obesity and associated metabolic abnormalities.<sup>6-8</sup>





### Biochanin A

**Biochanin A** is a plant flavone found in clover, peanuts, chickpeas, and soy.<sup>9</sup>

Research has found that biochanin A inhibits one of the enzymes in the endocannabinoid system called **fatty acid amide hydrolase**.<sup>10,11</sup> This enzyme breaks down the endocannabinoid anandamide into inactive products.

By *blocking* the activity of the enzyme, biochanin A may help to support *higher* levels of anandamide.<sup>12</sup>

**Anandamide** acts as a natural pain reliever in the body, so biochanin A may be useful in treating chronic pain and other conditions.<sup>11</sup>

Anandamide, through its function as a critical molecule in the endocannabinoid system, is also believed to play important roles in regulating motivation, pleasure, and mood.<sup>3,4,13</sup>

### Guineensine

A compound isolated from black pepper, **guineensine** boosts levels of both anandamide and 2-AG.<sup>14,15</sup> It works by blocking the reuptake of these endocannabinoids after their release by cells.<sup>16</sup>

As a result, levels of anandamide and 2-AG remain *higher* in the body for *longer*. Together with

biochanin A's ability to block anandamide's breakdown, this further boosts the beneficial effects of these endocannabinoids.

### Beta-Caryophyllene

**Beta-caryophyllene** is found in many plants, including rosemary, clove, and black pepper.<sup>14</sup>

Scientists have discovered that this compound directly activates one of the most important endocannabinoid *receptors*, known as **CB2**, mimicking the activity of some endocannabinoids.<sup>14</sup>

These CB2 receptors are found throughout the body. Their activation by beta-caryophyllene has been demonstrated to:

- Reduce inflammation in brain cells,<sup>17</sup>
- In an animal model, improve insulin function blood glucose control, lipids, and vascular inflammation,<sup>18</sup>
- Protect against age-related cognitive decline and reduce levels of an age-related proinflammatory cytokine,<sup>19</sup> and
- Inhibit breast cancer cell growth.<sup>20</sup>

## Summary

In the last few decades, scientists have discovered that the **endocannabinoid system** influences the balance and function of almost all bodily systems.

In the brain, it has important beneficial effects on mood, cognition, sleep, and more.

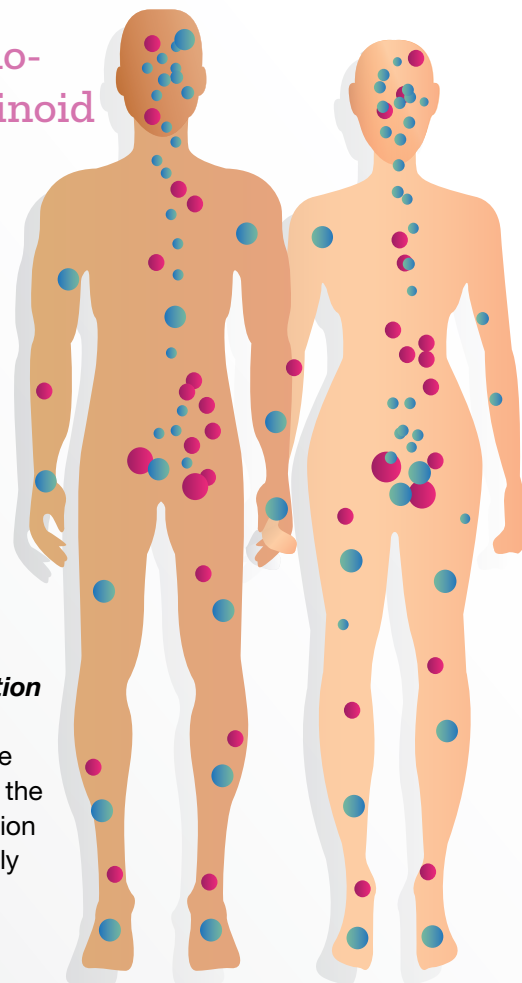
Throughout the body, it helps maintain tissue health, prevent age-related loss of function, and lower risk for disease.

Scientists have identified four plant-based compounds that influence the function of the endocannabinoid system: oleoylethanolamide (OEA), biochanin A, guineensine, and beta-caryophyllene.

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## The Endo-Cannabinoid System



A **cellular communication system** that helps regulate and maintain the optimal function of many bodily systems.

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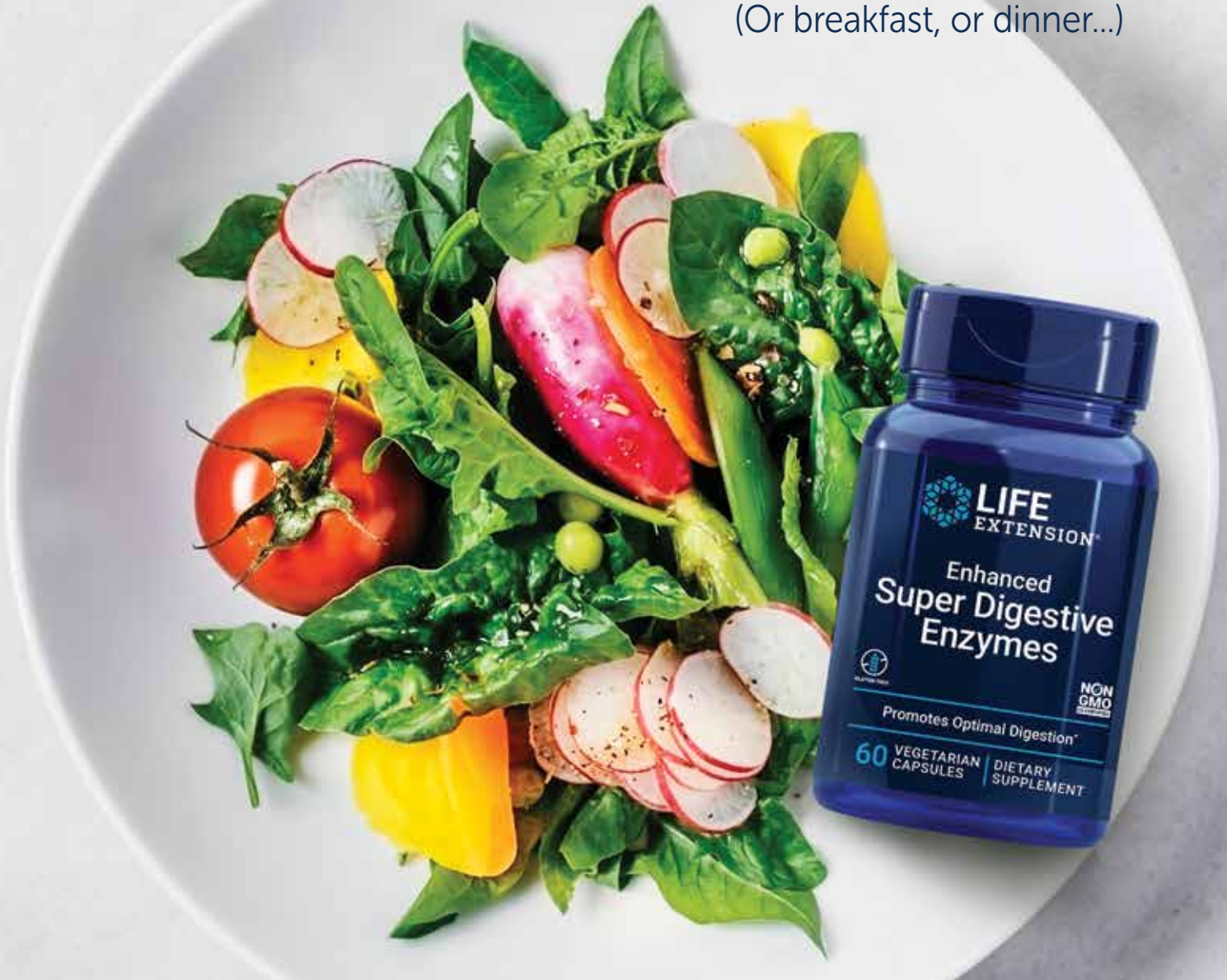


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A man with a beard and short dark hair, wearing a blue sweater over a white collared shirt, is shown from the chest up. He is holding a black smartphone in his right hand and pointing with his left index finger to his stomach. He has a watch on his left wrist. The background is blurred, showing what appears to be a social gathering with purple balloons. A semi-transparent blue banner is overlaid across the middle of the image, containing the title text.

# "Feed" Your Healthy Gut Bacteria





BY MICHAEL DOWNEY

Growing research shows that **prebiotics** are important “companions” to **probiotics** for optimal digestive health.

The gut microbiota, which are the trillions of microorganisms that reside in our gut, have been linked to mood, cardiovascular and gastrointestinal health, and the ability to ward off disease.<sup>1-4</sup>

Among the most important and beneficial gut bacteria are those belonging to the group **bifidobacteria**.<sup>5</sup>

Research shows that bifidobacteria have wide-ranging health benefits. They are associated with protection against allergies, high cholesterol levels, and respiratory diseases.<sup>6</sup>

With age, intestinal levels of beneficial bifidobacteria decline.<sup>6</sup>

To promote restoration of healthy **bifidobacteria** levels, scientists have identified a prebiotic called **xylooligosaccharide (XOS)**.

Even in low doses, it increases gut bifidobacteria in as few as **14 days**, without unpleasant digestive effects.<sup>7,8</sup>

**XOS** also reduces blood levels of cholesterol, triglycerides, and glucose.<sup>8</sup>

Taking oral **XOS** is a convenient and quick way to boost beneficial **bifidobacteria**.

## How Prebiotics Work

The trillions of microorganisms that reside in the human digestive tract—known as the gut **microbiota**—do much more than promote healthy digestion. They impact immunity, metabolism, the endocrine system, mood, and cardiovascular health.<sup>4,9-12</sup>

Foods that nourish and promote healthy gut flora are called **prebiotics**.

For a food ingredient to be classified as a prebiotic, it must:<sup>13</sup>

- Resist digestion,
- Be fermented by intestinal microorganisms, and
- Stimulate growth and/or activity of beneficial bacteria.

Most commercial **prebiotics** require large doses to provide optimal digestive health support. Unfortunately, this can cause excessive flatulence, bloating and general digestive discomfort.<sup>14</sup>

But years of research identified a prebiotic that works at extremely low doses. It's known as **XOS (xylo-oligosaccharide)**.

Even better, it specifically targets and boosts levels of **bifidobacteria**.



## Bifidobacteria Decline with Age

Levels of beneficial **bifidobacteria** decline *dramatically* with age.

In early adulthood, bifidobacteria make up **30%-40%** of our gut microbiota. Those levels fall to about:<sup>6</sup>

- **10%** by late middle-age, and
- Less than **5%** by old age.

Replenishing intestinal bifidobacteria restores their healthful effects on the body, while leaving less room for *dangerous* bacteria to take up residence.<sup>15</sup>

That's where **XOS** comes in. Made from non-GMO corn cobs, this prebiotic targets bifidobacteria, *preferentially* promoting their growth.

## XOS Boosts Bifidobacteria

Studies have demonstrated that **XOS** safely and significantly boosts levels of bifidobacteria.<sup>7,8</sup>

In one double-blind, randomized, placebo-controlled study, microbiologists and clinical researchers with the **UCLA School of Medicine** enlisted 32 healthy subjects and divided them into three groups.

Every day for eight weeks, one group took a **placebo**, the second took **1.4 grams** of XOS, and the third took **2.8 grams** of XOS.<sup>7</sup>

The preparation contained **70%** XOS, so that the total amount of XOS ingested in the two study groups was **1 gram** or **2 grams**, respectively.

Both treatment groups had *increases* in **bifidobacteria**, but those taking **2 grams** daily of XOS had significantly larger increases than the lower-dose group.<sup>7</sup>

To achieve similar increases using another common prebiotic, **FOS (fructooligosaccharides)**, you'd have to take **10 to 20 grams**, enough to cause cramps and other digestive problems.<sup>7</sup>

The XOS study found no significant side effects in any of the groups.

## Results in Just Two Weeks

Another team of scientists using the same doses of the *same* **XOS** preparation found that this prebiotic could significantly boost bifidobacteria levels in a much *shorter* time.<sup>8</sup>

The group taking **1 gram** of XOS daily saw significant increases in bifidobacteria in **28 days**.<sup>8</sup>

Those taking **2 grams** of XOS daily achieved significant increases in bifidobacteria in **just 14 days**.<sup>8</sup>



Why bifidobacteria respond so quickly and effectively to **XOS**, and at such low doses, is still being studied.

Research shows that bifidobacteria feed on precisely the types of carbohydrates that humans cannot digest, especially the group known as **oligosaccharides**.

**XOS** (xylooligosaccharide) is an important example of this group.<sup>16</sup>

### Benefits of XOS

Taking XOS and raising bifidobacteria levels results in wide-ranging health benefits.<sup>8</sup>

One study found that taking XOS led to gastrointestinal and metabolic improvements, including:<sup>8</sup>

- **Increased fecal acidity**, which inhibits less-desirable bacteria and promotes healthy bacteria,<sup>17</sup>
- **Decreased triglycerides and cholesterol** in the blood and increased levels in feces, and
- **Decreased blood sugar**, protecting against type II diabetes and metabolic syndrome.

## WHAT YOU NEED TO KNOW

### The Benefits of a Powerful Prebiotic

- The trillions of bacteria living in the human gut have an enormous impact on our health and vulnerability to disease.
- Higher levels of bifidobacteria are associated with resistance to a wide range of age-related diseases.
- A prebiotic called **XOS (xylooligosaccharide)** has been validated in human studies to specifically target and boost bifidobacteria. It works in very **low doses**, without side effects, in as little as **two weeks**.

A recent **2020** rat study found that **XOS** supplementation modulates gut flora and reduces colon inflammation caused by high-fat-diet-induced obesity.<sup>18</sup>

In addition, in treated rats XOS **counteracted the weight gain** induced by a high-fat diet and **decreased inflammatory factors** in the colon.

### Summary

The trillions of organisms that reside in the human digestive tract, or the gut microbiota, are a critical factor in sustaining our resistance to disease and promoting good health.

Among the most beneficial gut bacteria are those belonging to the group **bifidobacteria**.

With age, intestinal levels of these beneficial bacteria decline.

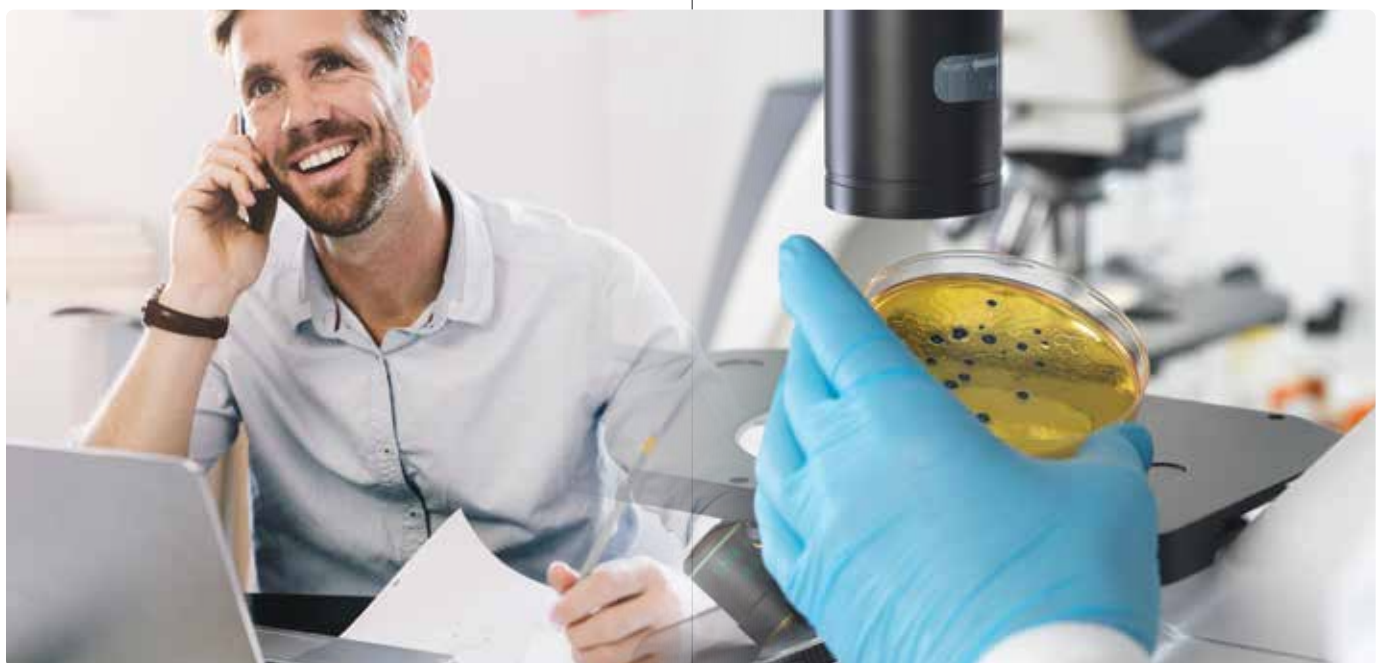
Scientists have identified a novel **prebiotic** called **XOS (xylooligosaccharide)** that has been shown in human clinical trials to boost bifidobacteria populations in the gut in as *little as two weeks*.

Unlike other prebiotics, XOS is effective in **low doses**, without side effects.

XOS has also been shown to lower cholesterol, triglycerides, and blood sugar, risk factors for cardiovascular disease and diabetes, respectively. •

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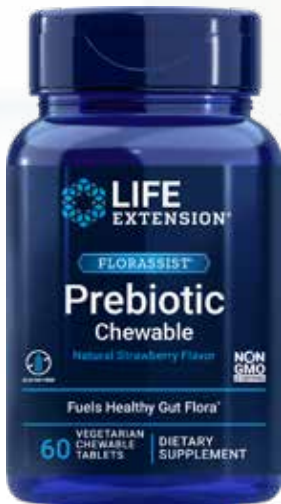
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1. *Front Microbiol.* 2016;7:1204.
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# Consumer Confusion about CHOLESTEROL *and* STATIN DRUGS

BY CHANCELLOR FALOON

**Statin** drugs remain controversial because they are often **overprescribed** and present side effects such as fatigue and muscle pain.

Few physicians advise their patients that statins deplete **CoQ10** from the body.

Restoring healthy levels of CoQ10 through supplementation has been shown to alleviate side effects as well as reduce the symptoms of **heart failure**.

If you or someone you know is on a statin, this article can help the patient and their physician make more educated decisions.

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## Statins and Heart Disease

**Heart disease** encompasses a range of cardiac disorders that include:

- Chronic **heart failure**
- **Coronary artery disease**
- **Valvular disease** (such as aortic stenosis)
- Sudden **heart attack**

Maintaining healthy levels of **cholesterol** is one way to help lower these risks.

There are people who question the evidence for the causal role of **LDL** cholesterol in atherosclerotic disease.

There is also disagreement about exactly which patient populations benefit most from cholesterol-lowering-type drugs called **statins**.

Concerns raised about **statin drugs** include:

- In people without known heart disease, there does not appear to be a mortality benefit with statin drugs, and the harms can outweigh the benefits,<sup>1,2</sup>
- Clinical trials of statins are largely industry-sponsored, and the original data in those studies are mostly unavailable to researchers,<sup>2,3</sup> and

- Lifestyle factors including tobacco usage, unhealthy diet, and sedentary lifestyle are thought to account for as much as **80%** of cardiovascular risk.<sup>2,4</sup>

The sum of published research shows that:

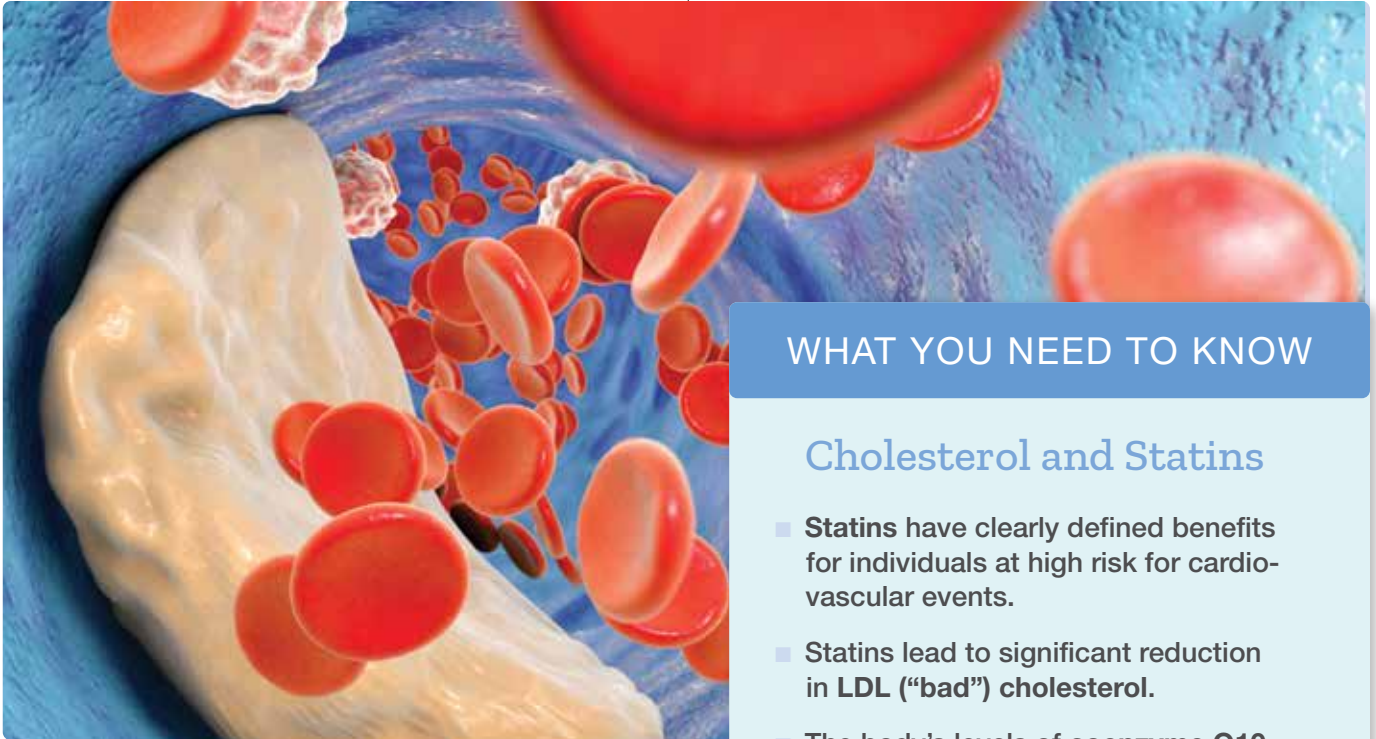
- Simple ways exist to diminish the most common statin-drug side effect,
- In high-risk individuals, statins *do* reduce heart disease deaths and mortality from other causes, and
- Comprehensive evaluation and control of cholesterol *and other* risk factors achieve the greatest reduction in heart disease risk.

Aging often results in an increase in **cholesterol**. This age-related increase in cholesterol is primarily composed of small, dense LDL particles, especially those oxidized, which promote the formation of harmful plaque in the arteries.<sup>5</sup>

As the decades add up, the damage inflicted by these cholesterol particles injures blood vessels, eventually obstructing blood flow to the heart muscle, brain, and other organs.<sup>6</sup>

If an aging individual with poor and worsening cholesterol does not want to make radical **lifestyle** and **dietary changes**, then proper **statin drug** therapy (usually at a much lower dose than commonly prescribed) should be considered.





## WHAT YOU NEED TO KNOW

### Cholesterol and Statins

- **Statins** have clearly defined benefits for individuals at high risk for cardiovascular events.
- Statins lead to significant reduction in **LDL** (“bad”) cholesterol.
- The body’s levels of **coenzyme Q10** are depleted by statins.
- Low **CoQ10** blood levels have been associated with *higher* mortality in **heart failure** patients.
- Statins interfere with the synthesis of **vitamin K2**, which helps promote arterial health.

### Reducing Statin Side Effects

**Cholesterol** is carried through the blood by transporters called **lipoproteins**, of which **LDL** (low-density lipoprotein) is one.

Statins lead to robust reductions in **LDL** (“bad”) cholesterol and decreases in **C-reactive protein**, a marker of **inflammation**.<sup>7</sup>

**Statins** have clearly defined benefits for **high-risk** individuals, but their use in **prevention** in **low-risk** individuals is not supported by that science.

Researchers and clinicians have pointed out that in individuals at **low** risk of cardiovascular events, side effects of statins outweigh benefits.<sup>1,8</sup>

**Life Extension**<sup>®</sup> was among the first to note that **statin drugs** were being overprescribed, often at unnecessarily **high** doses.

Statins deplete the body’s levels of **coenzyme Q10**, which causes many outward side effects, like muscle pain (myalgias) along with potential multi-organ damage.

Evidence also shows that statins interfere with the synthesis of **vitamin K2**.<sup>9,10</sup>

The encouraging news is muscle pain caused by statins can be significantly **reduced** with the addition of **coenzyme Q10**.<sup>11-14</sup>

The statin-induced **decrease** in **coenzyme Q10** and **vitamin K2** can be corrected by taking supplemental **CoQ10** and **vitamin K2**.

### CoQ10 Provides Support

A meta-analysis published in **2018** combined the results of **12 randomized, controlled trials** that included a total of **575** patients.

This study concluded that **coenzyme Q10 (CoQ10)** supplementation ameliorated the muscle pain, cramps, weakness, and tiredness associated with **statin** drugs. It also showed that **statins** reduce CoQ10 levels by **16%-54%**.<sup>14</sup>

In high-risk individuals (which includes a significant portion of the aging population), statin drugs help protect against cardiovascular disease,<sup>15</sup> including coronary artery occlusion and cerebral vascular insufficiency. In some observational studies, statin use showed potential in slowing aortic stenosis progression.<sup>16</sup> **Statins** also reduce CoQ10 levels.<sup>11</sup>



## New Data Support CoQ10's Protective Effects

A clinical trial published in 2019 (after the 2018 meta-analysis showing the CoQ10 protective effect in statin users), demonstrated another approach to protect against statin-induced myalgia:<sup>11</sup>

Cut the **statin drug** dose in half.  
+  
Add a **CoQ10** supplement.

In this study, 60 patients were selected who were all **statin intolerant** and had elevations in blood biomarkers (creatinine kinase and liver transaminases) which have been correlated with statin-induced muscle pain.

After patients were taken off statins for a month, they were then put back on a **half-dose statin** for a month. At that point they were randomized to receive either **100 mg of CoQ10** (ubiquinone) or a placebo. The difference was dramatic:

In the group that received the CoQ10, **46.6%** reported a reduction in pain scores.

In the group that received the placebo, only **6.6%** reported a reduction in pain scores.

Blood markers of **organ damage** sometimes seen in **statin drug** patients decreased significantly in the **CoQ10** group, while there was no significant change in biomarkers of muscle, liver, or kidney damage in the placebo group.

At the end of the study, participants in the CoQ10 group also had **lower LDL and total cholesterol** compared to the placebo group (not receiving CoQ10), and they accomplished this with just half the **statin dose** they were previously taking!

Low CoQ10 blood levels have been associated with **higher mortality** in **heart failure** patients.<sup>17</sup>

Continuing research shows that **CoQ10** supplementation can effectively boost levels of this heart-essential nutrient, improving outcomes for heart failure patients.

In a recent study, researchers selected 142 patients who developed **heart failure** while on statins.<sup>12</sup>

Of these patients, **94%** had **diastolic heart failure** (inability of their left ventricle to relax normally and properly fill) and **6%** had **systolic heart failure** (lack of their left ventricle contracting normally and pumping blood out into circulation).

The patients were taken off **statins** and put on an average dose of **300 mg/day** of **CoQ10**. The study primarily used the **ubiquinol** form of CoQ10, which is more readily **absorbed** into the bloodstream than ubiquinone.

By the end of follow-up (mean 2.8 years) the number of patients who had no limitations of physical activity increased from **8%** to an astounding **79%**.

For the patients with **diastolic** heart failure who received CoQ10, at final follow-up:

- Approximately **34%** had **complete normalization** of diastolic function,
- **60%** had sustained improvement in diastolic function, and
- **25%** showed improvement but not normalization of diastolic function.

For the patients who had **systolic** heart failure, **ejection fraction** increased by a mean of **12%**.

**Ejection fraction** is the percentage of blood pumped *out* of the heart's left ventricle with each beat. Measuring this percentage is essential to the proper evaluation and management of those with systolic heart failure.<sup>18</sup>

## Why Early Statin Trials Were Short Term

Some critics of statins contend the research does not consistently show they reduce cardiovascular or all-cause **mortality**.

However, real-world obstacles stand in the way of **long-term**, placebo-controlled human trials designed to test the effects of statins or other interventions on **mortality**, which is the proof we need to establish a life-extending benefit.

A study evaluating **human mortality** would require many decades to produce meaningful results. Humans live longer than lab animals, which makes us more difficult to study, and makes such research prohibitively costly.

Other factors add to the complexity. People often change their diet, exercise, and lifestyle habits. Compliance with any nutritional or pharmaceutical intervention tends to be inconsistent. Additional confounding factors that are difficult to control are stress levels, environment, and individual genetics.

For these reasons, long-term, randomized, placebo-controlled trials of potentially life-extending interventions—such as statins—present an enormous challenge to the scientific community.

### Newer Trials Show Reduced Mortality

But statin critics may be overlooking **newer** studies that *are* showing meaningful mortality benefits.

One large-scale meta-analysis published in **2016** showed that statins were significantly more effective for patients in reducing the odds of dying from coronary heart disease and from **any** cause, compared to control groups.<sup>21</sup>

Specifically, statin users had **31% lower** odds of dying from **coronary heart disease** and **16% lower** odds of dying from **any cause**, compared to controls.

### 20-Year Study Yields Robust Mortality Benefit

A study published in **2017** was one of the **first** to truly examine the impact of **statin** use over the **long term**.

This study analyzed evidence *after* the termination of a randomized, placebo-controlled statin trial. One arm of this study evaluated the effects of **statins** in men with LDL of **190 mg/dL** or higher and without preexisting vascular disease.

This analysis divided a total of 5,529 men into two groups, those with LDL levels **under 190 mg/dL** and those with LDL levels at **190 mg/dL** or higher.

The randomized, controlled phase of this trial was about **five years** and used a statin drug called **pravastatin**.

What makes this study significant is that the observational follow-up on patients was an **additional 15 years**, meaning the whole study population was followed for **20 years**.<sup>22</sup>

### Merck Received Patent for Combined Statin-CoQ10 Drug, but Never Brought it to Market

**Merck and Co., Inc.** is one of the world's largest pharmaceutical companies. It was the first to introduce a statin drug, called **lovastatin** (Mevacor®), in the 1980s and then another statin called **simvastatin** (Zocor®) in the 1990s.

In 1989, the company filed for a **patent** on a drug that **combined CoQ10** with a **statin** to reduce statin side effects. In **1990**, they were awarded that patent, which was scheduled to expire in 2009.<sup>19</sup>

Merck never proceeded with clinical trials needed for FDA approval.

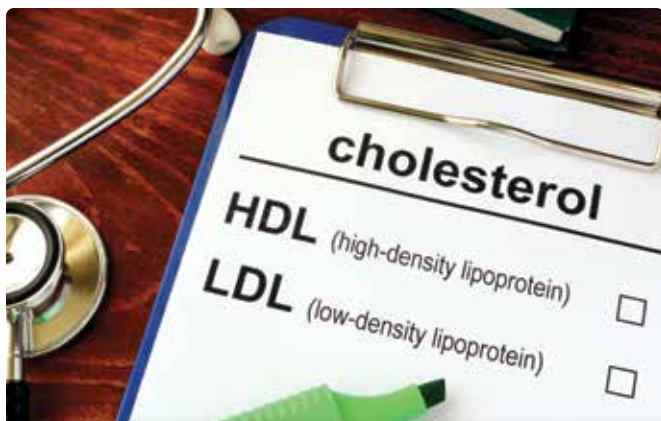
They may have decided that it was not worth spending hundreds of **millions** of dollars to conduct clinical trials and then develop a drug with CoQ10. Statin drugs are cheap to produce compared to coenzyme Q10, which is relatively expensive.

Merck's patent, however, kept other drug companies from pursuing a combination statin-CoQ10. Still, a survey published in 2015 reported that **71%** of cardiologists recommend CoQ10 to some of their patients.<sup>20</sup>



At the end of the **20-year** follow-up, an analysis was done comparing the placebo group to men with **LDL  $\geq$  190 mg/dL** and originally assigned to the **pravastatin** group in the initial trial. Here are the findings over this **20-year** period:

- The risk of coronary heart disease mortality was reduced by **28%** in pravastatin drug users,
- There was a **19%** reduced risk of major adverse cardiovascular events (defined as the composite of cardiovascular death, non-fatal heart attack, and non-fatal stroke), and
- Cardiovascular death was reduced by **25%** and all-cause mortality by **18%** respectively, in people remaining on pravastatin over this **20-year** period.



In the participants whose LDL was lower than **190 mg/dL**, deaths from all causes including cardiovascular disease were also lower in the **pravastatin** group compared to the placebo group. The participants with **LDL  $\geq$  190 mg/dL** had greater reductions in cardiovascular and all-cause mortality from **pravastatin** treatment compared to **placebo**.

The average LDL cholesterol level dropped by **23.3%** from its baseline value in the treatment group of those with **LDL  $\geq$  190 mg/dL**.

This **23.3%** reduction is still a considerable distance from what is generally accepted as a healthy **LDL range**, which is below **100 mg/dL** for primary prevention of cardiovascular disease in people with low risk.<sup>23</sup>

For people with high risk, such as individuals who have already suffered a cardiovascular event, some experts recommended that they achieve LDL levels below **70 mg/dL**.<sup>24</sup>

If LDL cholesterol had been brought down even further in the patients in the **20-year** study using **pravastatin**, the risk of cardiovascular events and all-cause mortality would likely have fallen with it.

It is important to note that these relatively recent studies were published *after* many decades of criticism were lodged against **statin drugs**.

No one questions the side effects statins can inflict. Much has to do with excess dosing and prescribing statins to patients who did not need them, and not advising patients to supplement with **CoQ10** and **vitamin K2**.

### Increased Risk When LDL Particles Are Small and Dense

A high number of **small, dense LDL particles** has been associated with elevated heart disease risk.<sup>30</sup>

The reason is that circulating, small, dense LDL particles easily penetrate and damage the blood vessel wall. In addition, they are more prone to atherogenic modification, including oxidation.<sup>31</sup>

**Oxidized LDL** damages the delicate endothelial cells lining the blood vessel wall.<sup>32</sup> Once the integrity of the endothelial barrier is compromised, additional oxidized LDL accumulates behind the arterial wall.

A critical step in the development of atherosclerosis is the adhesion of **monocytes** (a type of white

blood cell) to the **endothelial cells** that line the artery walls.<sup>33,34</sup>

These monocytes enter the blood vessel lining and develop into **macrophages** whose job is to engulf **oxidized LDL cholesterol**. Accumulation of oxidized LDL particles in the macrophage leads to the formation of **foam cells**.<sup>33,34</sup>

The accumulation of foam cells, along with the proliferation of smooth muscle cells and excess connective tissue, are key drivers of **atherosclerosis**.<sup>33,34</sup>

**Foam cells** play a central role in the inflammation that drives the **atherosclerosis** process.<sup>35</sup>

## Statins Improve Health Outcomes in US Veterans

A new study published in July 2020 in the *Journal of the American Medical Association (JAMA)* found that statin use was associated with substantial reduction in all-cause mortality.<sup>39</sup>

The study recruited 326,981 veterans with a mean age of 81 years and followed them for a mean of 6.8 years from a clinical visit.

Compared to non-statin drug users, statin use was associated with a 25% reduction in all-cause mortality, 20% reduction in cardiovascular mortality, and an 8% reduction in a composite of atherosclerotic cardiovascular events.

### Multiple Risk Factors for Cardiovascular Disease

There are some patients with high LDL cholesterol who do not have cardiovascular disease, while some with lower cholesterol do have it. These paradoxical findings have led some to downplay the risks posed by elevated **LDL cholesterol**. However, this does not mean that cholesterol plays no role in cardiovascular disease.

People sometimes forget that there are **multiple risk factors** contributing to the threat of every illness, and cardiovascular disease is no exception.

Scientific data accumulated over decades demonstrate that excess **LDL cholesterol** is one of the primary culprits.<sup>6</sup>

### Impact of Apolipoprotein B

**Apolipoprotein B** is found on all non-HDL-cholesterol-carrying lipoprotein particles, such as LDL and VLDL.<sup>25</sup>

High apolipoprotein B is a recognized marker for damage to arterial walls and risk of atherosclerosis. This is important because the basic laboratory tests for lipids, including LDL, HDL, and total cholesterol and triglycerides, often don't give the full picture of cardiovascular disease risk.

Research on certain populations shows a correlation between maintaining lifetime low levels of **apolipoprotein B** and a roughly **90% decreased** risk of coronary artery disease.<sup>26</sup>

Elevated **apolipoprotein B** is a more reliable marker for cardiovascular disease than **LDL, HDL, and total cholesterol**.<sup>6,27-29</sup>

Despite intensive educational efforts, **apolipoprotein B** blood tests are not routinely incorporated into primary care medicine. The tragic result is a failure to prevent heart attacks, strokes, and other occlusive arterial diseases.

For *Life Extension*<sup>®</sup> readers, this problem was resolved when **apolipoprotein B** was added to the comprehensive **Male** and **Female Panel** blood tests they undergo each year.

### Summary

Published data define the importance of maintaining optimal **LDL** and **HDL cholesterol** levels to lower heart disease risk.

**Statins** can help keep cholesterol levels in optimal ranges in those for whom diet and lifestyle measures aren't enough.

To achieve the most significant heart disease risk reduction, one must monitor and address every risk factor related to heart diseases. That includes testing for **apolipoprotein B** and other atherogenic risk factors.

Controlling the vascular damage created by elevated **LDL cholesterol** levels is challenging. Altering one's diet to reduce excess **saturated fat** intake might enable a **lower statin drug** dose to achieve optimal cholesterol levels.<sup>4,36-38</sup>

Anyone using a statin must ensure their **coenzyme Q10** levels are not compromised.

This can be achieved by taking **100-200 mg** a day of **CoQ10**, preferably the **ubiquinol** form. CoQ10 should be taken with the heaviest meal of the day that contains some fat, to facilitate its absorption.

Those with **heart failure** usually need to take around **400 mg of ubiquinol** a day to achieve optimal CoQ10 blood levels.

Recent data also point to the value of **vitamin K2** use with statin drugs. For those interested in supplementing with vitamin K who are taking Coumadin<sup>®</sup> or Jantoven<sup>®</sup> (warfarin), please discuss with your doctor first. The box on the next page describes what some warfarin users are doing to supplement with **low-dose** vitamin K2 under physician supervision.

These steps can lessen the side effects of **statins** and help to lower the risk of cardiovascular disease.

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## Vitamin K Antagonists, Food Sources of Vitamin K, and INR Variability

Warfarin is a drug that inhibits unwanted coagulation by interfering with vitamin K activity in the liver.

A frequently encountered problem with patients prescribed warfarin, a vitamin K antagonist, is the **variability** of INR.

INR (international normalization ratio) is a measurement of warfarin's effect upon the tendency of the blood to clot through the extrinsic clotting pathway. This can be due to variation of dietary intake of rich food sources of vitamin K (e.g. green leafy vegetables).

Too much vitamin K can **diminish** the **anticoagulant** effects of warfarin and produce **unstable** INR measurements.

In patients receiving warfarin with a goal INR of 2-3, the addition of low-dose oral vitamin K supplementation may help **increase** INR stability.

Some published research suggests that low-dose (around 45 mcg) vitamin K may help improve the stability of INR measurements—however, such a strategy should only be contemplated after full discussion with a patient's physician and frequent blood testing (to include INR) to assess for the intended effect (i.e. INR stability).

Warfarin users seeking more details about this should log on to: [LifeExtension.com/warfarin](http://LifeExtension.com/warfarin)

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# Cardiologist Observes Improved Patient Outcomes & Reversal of **Calcification** and **Atherosclerosis**

JOEL KAHN, MD

I have devoted my career as a cardiologist to finding ways to treat **atherosclerosis**—the buildup of **plaque** in artery walls.

I've relied primarily on healthy lifestyle changes, diet, and supplements.

A few years ago, a **human** study found that a combination of two **plant extracts** significantly reduced **arterial plaque** in the carotid arteries when added to diet, exercise, and healthy lifestyle counseling.<sup>1</sup>

I have recommended these plant extracts to thousands of patients and have seen the favorable results firsthand.

Larger studies provide new evidence that arterial **calcification** and blockages are reversible.

## My Clinical Practice

I spent seven years after medical school completing my training in **interventional cardiology** or using catheters to treat heart disease.

Much of my practice involved inserting **stents** to prop open **coronary arteries** that were occluded with **atherosclerotic** plaque.

But three weeks into my first job, I decided there was a better, more comprehensive approach.

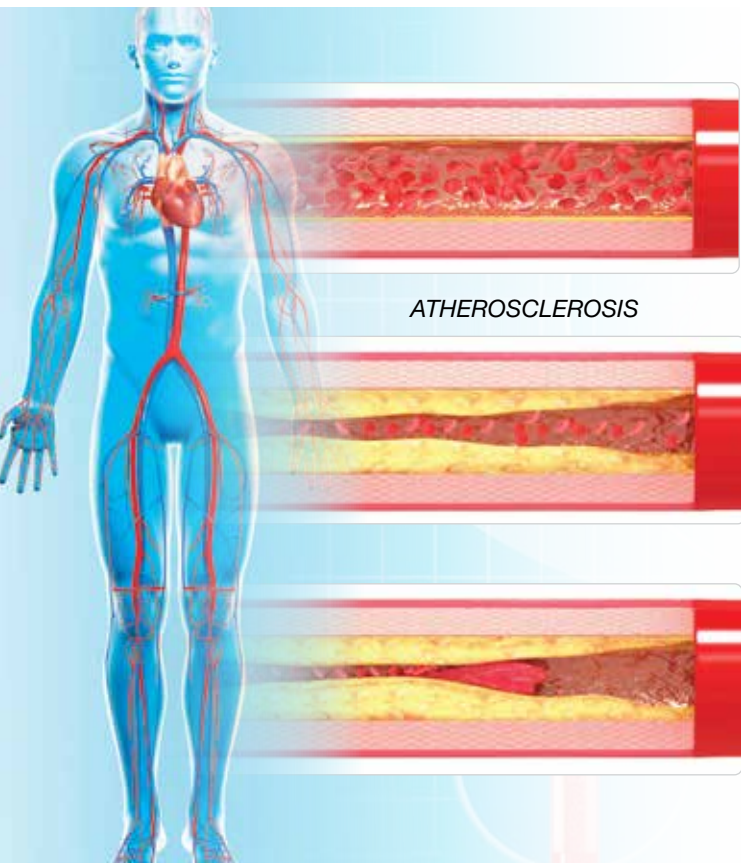
At that time, I read a study in a respected medical journal focusing on **atherosclerosis**, which often leads to heart attacks and strokes.

The study reported that atherosclerosis had been reversed using lifestyle and diet changes.<sup>2</sup>

Since then, I've combined **interventional cardiology** with a search for lifestyle and supplement-based methods to stabilize and reverse plaque buildup.

I was particularly impressed by a published study that reported on a combination of extracts of **French maritime pine bark** and an herbal extract called **Centella asiatica**.

When added to standard diet, exercise, and lifestyle counseling, these two **plant extracts** improved plaque stability and reduced size and numbers of **arterial plaques**.<sup>1</sup>



The study involved 50 patients with plaque in the **carotid arteries**, which supply blood to the brain, neck, and face. These patients had no history of cardiovascular events, and did not have diabetes or metabolic problems.<sup>1</sup>

Over the three-month study period, **pine bark + Centella asiatica** extracts reduced **carotid artery plaque** and lowered the **number of plaques** compared to a control group.

After these scientific findings were published, this **pine bark-Centella** extract combination became a routine part of my atherosclerosis reversal program.

## The Evidence Mounts

I grew more convinced of the effectiveness of this plant combination when a larger, longer-term study was published in **2017**.<sup>3</sup>

This time, 391 subjects were followed for **four years**.

All had asymptomatic atherosclerosis of either the **carotid artery** or the **femoral artery** (which provides blood to the leg). Atherosclerotic lesions extended **50%-60%** into the arteries in at least one location.

Three treatment groups were formed. One was treated with extract of **pine bark** alone, another was treated with **pine bark** and **Centella asiatica**, and a third control group received no extracts. All groups received standard diet, exercise, and lifestyle counseling.

The rate of plaque progression, measured by ultrasound, was significantly lower in both treatment groups than in the control group. The group that took the combination of the two extracts had the greatest reduction in progression of plaque thickness and length.

The extracts also had a favorable impact on cardiovascular outcomes as follows:

- The occurrence of **angina**, chest pain caused by reduced blood flow to the heart, was less than **3%** in the two **extract** groups, compared with **6.25%** in control patients.
- The rate of **heart attacks** was significantly lower for the combination therapy.
- Events requiring **hospital admission** occurred in **16.4%** of control subjects, **8.9%** of subjects using only French maritime **pine bark** extract, and **just 3.3%** of patients using the combination of **pine bark** and **Centella extracts**.

## Pine Bark - *Centella* Extracts in Practice

I have used this combination with countless patients in my clinic who have plaques clogging their carotid arteries.

I use the **carotid intima-media thickness** (ultrasound) test to identify and track carotid plaque status.

This test measures the thickness of the inner layers of the carotid artery, the **intima** and the **media**.<sup>4</sup>

*Increased* plaque means *greater* thickness, enabling this carotid ultrasound test to reveal atherosclerosis even in people with no symptoms.

I routinely observe reversal of plaque in patients taking the **pine bark + *Centella* extract** combination. I have even seen **arterial age** drop **10 to 20 years** after only one or two years of therapy.

## Preventing Arterial Plaque Progression

My use of these extracts has recently expanded *again*, based on data published in **2020**.

This Italian trial involved 84 normal weight to mildly overweight subjects with asymptomatic **atherosclerosis** in their **carotid** and **femoral arteries**, determined by high-resolution ultrasound.

These atherosclerotic subjects were treated with similar interventions as the studies already discussed. The duration of this trial was three years.<sup>5</sup>

Patients with an atherosclerotic plaque that was blocking less than **50%** of an artery and those with an atherosclerotic plaque blocking more than **50%** of an artery were included in this trial.

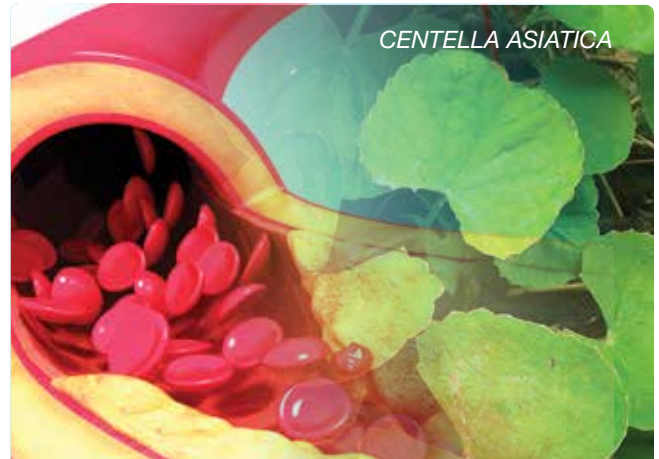
All patients were given diet, exercise, and lifestyle counseling.

One group received no additional treatment, a second took **100 mg** a day of **aspirin**, and a third received the aspirin plus the combination of extracts of French maritime **pine bark (150 mg/day)** and ***Centella asiatica* (450 mg/day)**.

At the end of the three years, more than **20%** of patients in the **standard management** and the **aspirin** group had progressed to more severe and extensive atherosclerotic plaque.

Among patients treated with **aspirin + pine bark + *Centella***, only **5.3%** of patients experienced **plaque progression**.

In the diet, exercise, and lifestyle-counseling group, **22%** suffered a cardiovascular event requiring hospitalization. That number declined to **12%** in the **aspirin** group and to just **3.5%** in the group taking aspirin plus the two **plant extracts**.



## WHAT YOU NEED TO KNOW

### Reducing and Reversing Plaque Progression

- **Atherosclerosis** is the buildup of **plaque** in artery walls.
- A combination of two **plant extracts** significantly reduced **arterial plaque** in the carotid arteries.
- **French maritime pine bark-*Centella asiatica*** extracts prevent plaque progression.
- This combination of plant extracts may reverse the progression of **atherosclerosis**.

Oxidative stress, a driver of atherosclerosis, was measured in the blood of all subjects and was lower in the group taking the **pine bark** and ***Centella*** extracts. This makes sense since both these plant nutrients are free-radical scavengers.

### Decrease of Coronary Artery Calcification

The same research team evaluated the efficacy of the **pine bark-*Centella*** combination in asymptomatic atherosclerotic patients with coronary artery **calcifications**.<sup>6</sup>

Patients with atherosclerosis in the **coronary arteries**—those that supply the heart with blood—can experience angina, shortness of breath, and even a heart attack.<sup>7</sup>

The study included three groups of 30 men each with asymptomatic **coronary artery calcifications**. Although they didn't have angina or shortness of breath, the **calcification** in their arteries indicated progressive atherosclerosis.

All subjects received standard diet, exercise, and life-style counseling and took **100 mg/day** of aspirin.

The first group received no additional treatment. The second added **150 mg/day** of French maritime pine bark extract. The third used the combination of **150 mg/day pine bark** and **450 mg/day of *Centella asiatica*** extracts.

After one year, there was a **35% increase** in the number of coronary artery calcifications in the group that received diet, lifestyle, and exercise counseling plus aspirin. In those also taking **pine bark** alone, new **calcifications** were **halted**.

In those using the **pine bark + *Centella*** there was a significant **10% decrease** in the number of **calcifications**, a remarkable result.

### Testing in Patients with Stents

To evaluate the impact of **pine bark** and ***Centella asiatica*** extracts on atherosclerotic plaque progression in **stented arteries**, 160 stented patients with partial arterial blockage due to atherosclerotic changes (as determined by ultrasound) were grouped into one of three treatment arms.<sup>8</sup>

The study began 6-10 months after successful **stent** procedures, and patients were followed for 12 months.

All groups received diet, exercise, and lifestyle advice along with anti-platelet medication and low-dose statin. A second group received, in addition, the **pine bark extract**; and a third group received extracts of **pine bark** and ***Centella***.

After 12 months, progression of atherosclerotic lesions on inner artery walls occurred in **6.7 times more** patients in the diet, exercise, lifestyle, and medication only group compared to the group that **also** received the combined **pine bark + *Centella*** extracts.

In fact, in just one year, **nearly 60%** of patients in the group that did **not** receive **the plant extracts** had marked progression of their **atherosclerosis**.

By contrast, among subjects who received the additional **pine bark extract** without ***Centella***, only **18.5%** experienced atherosclerosis progression.

Most remarkable of all, though, were the results in the **pine bark + *Centella*** extracts group. Just **8.9%** of these patients had progression of **atherosclerotic plaques**.

In both groups that received extracts, there was a significant reduction in oxidative stress. No side effects or tolerability problems were observed with the plant extracts.

### Summary

These studies consistently show that the combination of **French maritime pine bark** and ***Centella asiatica*** extracts slows and may reverse the progression of **atherosclerosis**.

The published findings reveal significant reductions in adverse **cardiovascular outcomes**.

I've observed these powerful results in my clinic as well.

The combination of these **plant extracts (pine bark + *Centella*)** has promise for millions of people with atherosclerosis. •

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Joel Kahn, MD, is the founder of the Kahn Center for Cardiac Longevity in Bingham Farms, Michigan.

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



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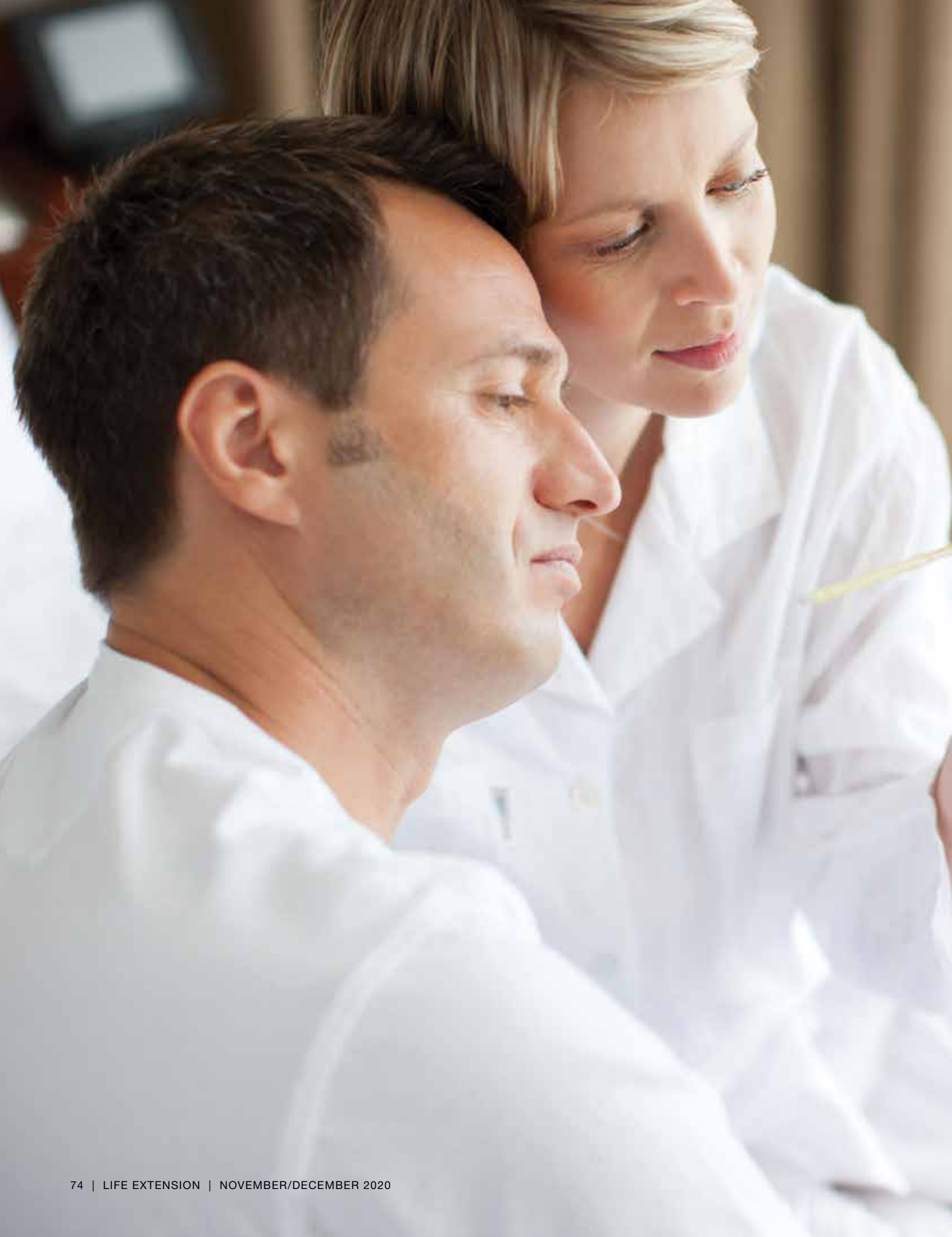
\* *Int Angiol.* 2014 Feb;33(1):20-6.

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# *Enhanced* IMMUNITY *Against* ALLERGIES *and* COLDS

BY MICHAEL DOWNEY

**Allergies** and **colds** affect people of various age groups.

Drugs target symptoms without correcting underlying causes of these miseries.

Scientists have discovered two ingredients that *reduce the severity* of allergy and cold symptoms and help **prevent them** from occurring.

**Human** studies show that these ingredients lead to:<sup>1-3</sup>

- **55% decreased** cold and flu occurrence,
- **43% fewer** days with nasal congestion,
- **17% reduced** duration of cold and flu-like symptoms, and
- **47% increased** salivary **immunoglobulin A**, an antibody that provides immune defense against viruses and bacteria.

This article describes how one may reduce frequency and duration of allergy and cold symptoms.



### Colds, Allergies, and Other Infections

American adults get an average of **two to three colds** annually,<sup>4</sup> and as many as **30%** of U.S. adults suffer from **allergies**.<sup>5</sup>

Sometimes it feels like we spend half our lives sneezing, coughing, and blowing our noses. This has a major impact on quality of life, but there's a more serious danger: Allergies have been associated with other conditions, such as asthma, and sinus and ear infections.<sup>6,7</sup>

### Preventing and Reducing Symptoms

Medications provide mild relief of symptoms but do nothing to reduce the number of colds and allergy bouts per year or how long they last.

Side effects from these drugs can include drowsiness, constipation, headaches, rapid heartbeat, and sleep problems.<sup>8</sup> One class of allergy drugs, **anticholinergics**, has even been linked to an increased risk of Alzheimer's disease.<sup>9</sup>

Scientists have identified two ingredients that help prevent colds, flu, and allergic episodes, and lessen the severity and duration of symptoms when they *do* occur.<sup>1-3</sup>

The ingredients are:

- A dried **yeast fermentate** and
- A probiotic called ***Lactobacillus rhamnosus* CRL1505**.

Each of these ingredients boosts activity of **immunoglobulin A (IgA)**, an antibody that provides immune defense against viruses and bacteria.<sup>3,10</sup>

### Discovery of Yeast's Immune Benefits

The immune effects of **yeast fermentate** were discovered by accident.

A company in Cedar Rapids, Iowa, had been producing a specialized yeast culture when it became apparent that its factory workers—who were exposed to the yeast daily through inhalation—were taking far fewer sick days than its office workers.

Scientists took note. A pilot study showed that, compared to the office staff, the factory personnel had significantly *higher* levels of **secretory IgA**, an **antibody** that blocks pathogens from penetrating **mucosal** surfaces.<sup>11</sup>

They also had increased activity of **natural killer cells**, immune cells that can kill cells infected with viruses.<sup>12</sup>

The company went on to develop the **dried yeast fermentate** using a proprietary fermentation process and baker's yeast. At least six placebo-controlled **clinical trials** have since validated its protection against allergies and colds.<sup>1,2,10,13-15</sup>

## Defense Against Allergies

Scientists first conducted a small pilot study on 25 healthy individuals, giving them either a **placebo** or **500 mg** of dried **yeast fermentate** daily for five weeks during the beginning of allergy season.<sup>10</sup>

Seasonal allergies did not change in the **placebo** group.

In the group taking the **yeast fermentate** there were improvements. **Half** of the treated male volunteers reported a **complete absence of allergy symptoms**, which returned within two weeks once they stopped taking the yeast fermentate.<sup>10</sup>

Researchers then conducted a clinical study on 96 volunteers with a history of seasonal allergies and hay fever. Participants took either a placebo or **500 mg** of dried **yeast fermentate** once daily.<sup>1</sup>

The first six weeks of the 12-week study took place during the year's highest pollen-count period. Compared to the placebo group, those taking yeast had **43% fewer days** with **nasal congestion**. They also had a reduction in the *severity* of runny noses and nasal congestion.

By the study's end, those taking yeast fermentate showed decreased levels of white blood cells in their nasal mucus, indicating reduced activation of allergy-triggering cells.<sup>1</sup>

## Yeast Fermentate Fights Colds and Flu

Scientists next set up two clinical studies to examine yeast fermentate's effect on **cold** and **flu-like** symptoms.

In the first, they gave a daily dose of **500 mg** of dried **yeast fermentate** to 116 people with a mean age of 37. The 12-week trial was conducted from January through March, during the height of cold and flu season.

At the end of the study, the yeast group had experienced a **13% reduction** in the occurrence of cold or flu-like symptoms (including headache, fever, general aches and pains, fatigue, nasal stuffiness, sore throat, cough, and chills) compared to the placebo group.<sup>14</sup>

The second study was virtually identical to the first, except that the 116 participants had an average age of 44. They received the same dosages of the dried yeast fermentate or a placebo and recorded the incidence and *duration* of symptoms.<sup>2</sup>

Compared to the placebo group, the yeast-treated group had **11% fewer** incidences of common cold or flu-like symptoms, and a **17% reduction** in the *duration* of symptoms.

## WHAT YOU NEED TO KNOW

### Defending Against Allergies, Colds, and Infections Year-Round

- Clinical studies show that a **yeast fermentate** and the probiotic *Lactobacillus rhamnosus* CRL1505 decrease the frequency, duration, and severity of allergy and cold symptoms.
- These ingredients also boost **natural killer cell activity** and **immunoglobulin A (IgA)** immune defenses against viruses and bacteria.
- Combining these two ingredients provides a safe and effective way for cold, flu, and allergy sufferers to improve their quality of life and may reduce risk of infection.



### How Yeast Fermentate Works

Antibodies called **immunoglobulin E (IgE)** are a main cause of allergy symptoms. IgE causes the body to release chemicals, such as **histamines**, that trigger an allergic reaction and produce symptoms that affect the eyes, nose, throat, lungs, or skin.

In the small pilot study that first showed **yeast fermentate's** ability to relieve allergy symptoms, blood levels of **IgE** steadily *increased* among placebo recipients as allergy season went into full swing, indicating heightened allergic responses.

In subjects taking the yeast, **IgE** levels barely changed, indicating a *reduced* allergic reaction.

The study concluded that **yeast fermentate** calms allergic responses by **stabilizing IgE** levels.<sup>10</sup>

Yeast's ability to help prevent colds and flu comes from a different property. When given a single dose of **500 mg** of dried yeast fermentate, volunteers had significantly *increased* activity of **natural killer cells** within just one hour.<sup>13</sup> These immune cells specifically target and kill cells infected by viruses, such as those that cause colds and flu.

Healthy individuals given **500 mg** of yeast fermentate daily also had a significant *increase* in **salivary IgA**, which defends against viruses and bacteria, after eight weeks.<sup>10</sup>

### A Probiotic's Cold and Flu Defense

**Probiotics** are beneficial live microorganisms. A specific strain of probiotic, the bacterium ***Lactobacillus rhamnosus* CRL1505**, was originally isolated from goat's milk by scientists in northwestern Argentina.<sup>16</sup>

A series of studies showed that it decreased **respiratory infections** in children. Results were so impressive, the government of Argentina has been proactively providing *L. rhamnosus* CRL1505 to over 300,000 school children annually since **2008**.<sup>3,16,17</sup>

Preclinical studies show that this probiotic strain may help fight the viruses and bacteria that cause the **common cold, influenza, bronchitis, and pneumonia**.<sup>17,18</sup>

A team of nutritionists, pediatricians, and immunologists designed a randomized, double-blind, placebo-controlled clinical trial. They enlisted 298 healthy male and female children between two and five years of age.<sup>3</sup> This population is particularly susceptible to respiratory infections.

Five days a week, the treatment group was given **100 million CFU** (colony-forming units) of ***L. rhamnosus* CRL1505** in a yogurt drink. The **placebo** group received a drink without the probiotic.







After six months, when compared to the placebo group, the children in the **probiotic** group had experienced:<sup>3</sup>

- **49%** fewer infections,
- **55%** fewer cases of cold or flu,
- **46%** fewer cases of fever,
- **47%** increase in levels of salivary IgA, and
- **33%** less need for antibiotic use.

The treatment group also had **61% fewer** cases of **tonsillitis** and **pharyngitis**, an infection in the back of the throat.<sup>3</sup>

### How the Probiotic Works

**IgA** antibodies are a major part of the immune system. Secreted from **mucous membranes** in the mouth, nose, and lungs, they bind to respiratory viruses, *blocking* them from invading human cells and producing symptoms of colds and flu.

Research shows that ***L. rhamnosus* CRL1505** significantly *increases* levels of secretory IgA,<sup>3</sup> boosting the immune system's initial ability to fight cold and flu viruses.

Along with yeast fermentate, this probiotic has demonstrated a reduction in severity, frequency, and duration of cold and flu symptoms and may offer protection against infections.

### Summary

**Allergies** and **colds** are more than an inconvenience. Human studies show that a **yeast fermentate** and the probiotic ***Lactobacillus rhamnosus* CRL1505** reduce the severity, occurrence, and duration of allergy, cold, and flu-like symptoms.

These two ingredients work in multiple ways to enhance **immune defenses** against viruses *and* bacteria.



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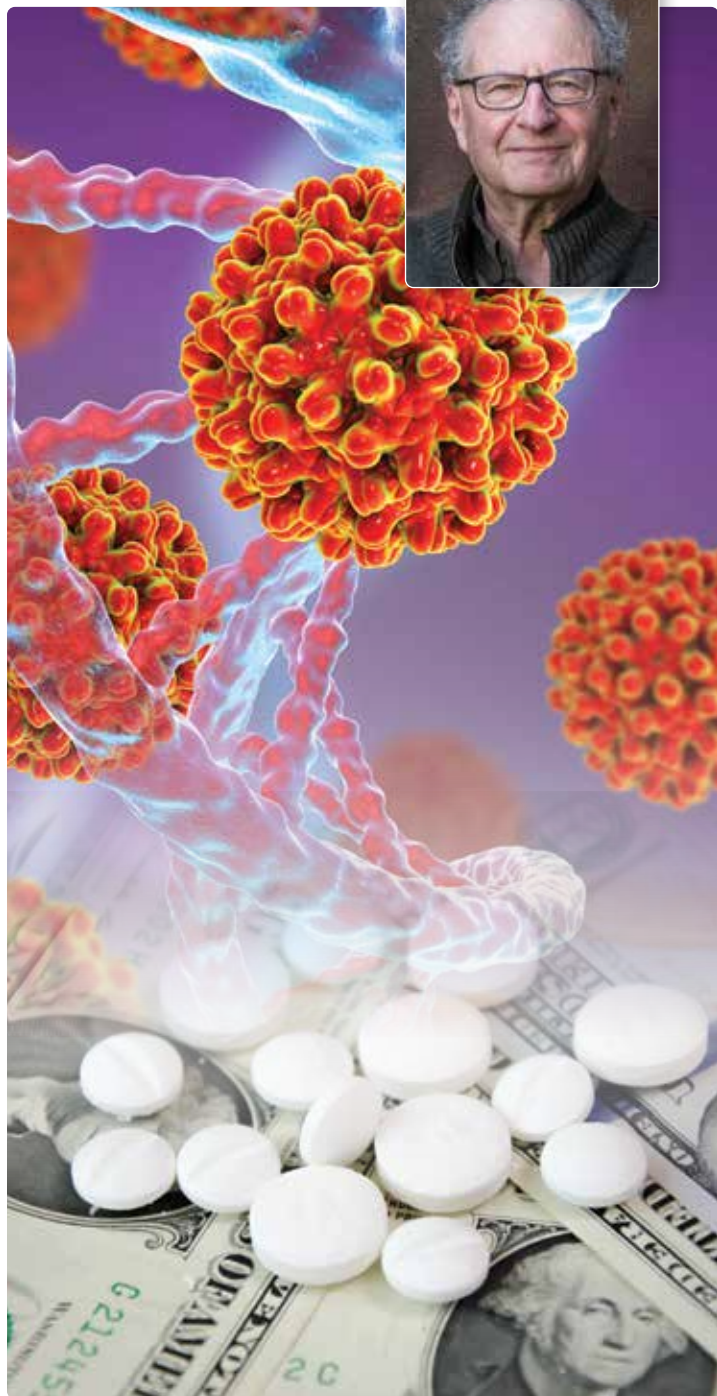
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# Cancer, Incorporated

*Inside Story of Corruption, Greed & Needless Deaths*

BY RALPH W. MOSS, PHD



Dr. Ralph Moss is a renowned investigative medical journalist who has been exposing corruption within the cancer industry for over 40 years.

While working at Memorial Sloan-Kettering Cancer Center in the 1970s, he blew the whistle when the favorable results of a plant-based substance were covered up.

He was promptly fired.

Since that time, Moss has written 12 books and countless articles, and been featured on radio, webcasts, and TV shows, including “60 Minutes.”

In his latest book, ***Cancer, Incorporated***, Moss is once again calling attention to the corruption and lies that are the true “cancer” in the cancer industry, including the “revolving door” that exists between “**Big Pharma**” and the **FDA**.

He reveals the inside story of how the pharmaceutical industry has managed to manipulate every aspect of drug development and has bought and paid for good opinions about mediocre drugs by key oncology leaders.

He also provides evidence of how Big Pharma has paid millions to doctors to downplay drug side effects and play up non-existent benefits in rigged clinical trials.

In this interview with ***Life Extension***<sup>®</sup>, Moss discusses how Big Pharma has hijacked the clinical-trial system, resulting in a flood of unproven, highly toxic, and outrageously priced drugs that have little to no benefit for the average patient.

—LAURIE MATHENA

**LE:** Are we making progress in the war against cancer?

**Dr. Moss:** We are told that steady progress is being made. In particular, it is said that the current system is producing effective ‘targeted’ drugs almost every day. New drugs are bringing a supposed “world without cancer” into view.

This is wishful thinking.

In fact, there is massive deception and manipulation underway, to convince us that steady progress is being made.

This is to get us to continue to consume—in fact, to demand—the products of the pharmaceutical industry, and to keep us from investigating less profitable treatments that could upset the multi-billion-dollar plans and ploys of the drug industry.

**LE:** What did a study published in the *Journal of Clinical Oncology* reveal about the effectiveness of conventional cancer drugs?

**Dr. Moss:** The authors reviewed 570 phase II single-agent studies involving over 30,000 patients, that were published between 2010 and 2012. They then looked at the response rates, progression-free survival and overall survival.

When it came to non-personalized cancer treatments, the results in numerous phase II trials were shocking:

1. The median overall response rate (tumor shrinkages) was **10.5%**.
2. The median progression-free survival was 2.7 months.
3. The median overall survival was 8.9 months.

Almost nothing that oncologists did would budge cancer’s stubborn bottom line.

But there was worse news. Even using the most advanced techniques, at some of the world’s finest hospitals, some patients were still dying from the treatment itself.

In these carefully controlled clinical trials, with billions of dollars riding on the outcome, the drug-related death rate on average was **2.3%**. The authors suggested the obvious, that this was “perhaps because of the known adverse effects often accompanying the administration of cytotoxic agents.”

**LE:** How has Big Pharma changed what it means for a drug to be “effective”?

**Dr. Moss:** Very few treatments are proven to deliver any actual benefit to cancer patients. That is because they are based on dubious measurements, or what scientists call surrogate endpoints.

The *NCI Cancer Dictionary* defines a surrogate endpoint this way: “In clinical trials, [it is] an indicator or sign used in place of another to tell if a treatment works. Surrogate endpoints include a shrinking tumor or lower biomarker levels. They may be used instead of stronger indicators, such as longer survival or improved quality of life, because the results of the trial can be measured sooner.”

The use of surrogate endpoints may increase the speed and efficiency of getting new drugs to market. But many experts warn that these surrogate endpoints have little or nothing to do with actual patient benefit.

From the beginning, shrinking tumors was not a major goal itself, but simply a convenient tool for tracking a drug’s contribution to the real goal, which is increased overall survival with a good quality of life.

Surrogate endpoints are thus not a sufficient basis for the FDA to approve a new drug. They are not true indicators of how well a treatment works but are in fact



unreliable substitutes that allow drug companies to gain rapid approval of unproven remedies.

**LE:** Why does Big Pharma rush the approval process, and why does the FDA allow accelerated approvals?

**Dr. Moss:** In drug development, every month counts.

The profitability of a new drug is based on the company's exploitation of its patents. A patent excludes anyone else from marketing that agent for 20 years. It is a legal monopoly. During that time, according to current U.S. law, one can charge patients whatever the market will bear.

It is not only cheaper to do smaller phase II trials, but such trials are much quicker to perform. A phase II trial generally takes about two years, while a phase III trial can take up to five. So, naturally, companies, and Big Pharma in general, are always trying to shorten the testing period by weakening the FDA's requirements of proof.

It is often claimed that the FDA lowered its standards in order to speed effective new drugs to market. This was the takeaway message from the HIV/AIDS pandemic.

But fewer than half of the cancer drugs it approves actually extend survival, even by as little as one month. The other approvals merely promote the bottom line of Big Pharma, while providing an illusion of effectiveness to patients and doctors.

Since 1992, [the FDA] has given accelerated approval to drugs based on dubious markers of alleged benefit.

Why have they lowered their standards in this way? To quote *MedPageToday*: "The FDA does not make decisions in a vacuum—it is under constant pressure from

## Moss Reports

Dr. Ralph Moss is best known for his highly informative **Moss Reports**. These 500+ page documents include expert analysis on 38 of the most common types of cancer.

Each Moss Report covers topics ranging from conventional treatments to alternative treatments, and from naturopathy to supplements. They answer key questions like which hospitals are most experienced in specific kinds of cancer, the best diet for healing your body, and which supplements are the most beneficial.

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For more information, visit [www.MossReports.com](http://www.MossReports.com).

politicians, pharmaceutical companies, and advocacy groups to speed up the drug approval process."

**LE:** How are clinical trials rigged against the older population?

**Dr. Moss:** Cancer is largely a disease of seniors. At the same time, seniors only represent one third of the adult participants in cancer clinical studies.

What impact does advanced age have on the outcome of trials? Elderly people in a clinical trial are at increased risk of more frequent and severe side effects and are therefore more likely to need delays in their treatment or might even drop out or die.

There is evidence that many cancer drugs do not work as advertised in older patients. For example, a 2018 study of the cancer drug Xeloda found that patients aged 70 years or older experienced more serious adverse effects than younger patients. The drug dosage had to be reduced in one-third of the younger patients versus in **82.5%** of the elderly ones.

In cases like this, the severe side effects of an experimental treatment almost certainly led to the death of

some older participants. Beside the human tragedy, this would depress the survival rate and possibly cause a delay, suspension or cancellation of the trial. Thus, a drug's proponents have a practical reason to keep the elderly out of their trial.

A 2018 study at The Mount Sinai Hospital, New York, found that elderly patients with metastatic bladder cancer who were treated in the community setting did much worse than patients enrolled in a clinical trial. Elderly patients treated in the community setting who were receiving chemotherapy had a survival of 8.5 months. But in the clinical trial, the median overall survival was 18.5 months.

At the very least, one cannot assume that a treatment that was approved based on a younger population will perform as expected in older people.

**LE:** Of course, there are financial ties between Big Pharma and medical doctors as well. Is anyone keeping tabs on this?

**Dr. Moss:** For details on payments by Big Pharma to American doctors you need to consult a U.S. government website named Open Payments.



Open Payments keeps track, to the penny, of the money that flows from Big Pharma to doctors and hospitals across the U.S. It makes that information freely available to the general public in an admirably transparent way. So, people who are interested in understanding oncology's relationship to Big Pharma should familiarize themselves with this invaluable site.

Dr. Vinay Prasad has called Big Pharma money paid to doctors "the cancer growing in cancer medicine." He does not exaggerate.

At this time, Open Payments provides information for the years 2013 through 2018. This shows that during this five-year period Big Pharma paid out \$43.22 billion dollars in numerous transactions with American doctors and hospitals.

To be clear, this is not a payment for goods or services in the normal sense. It is mainly for the purchase of goodwill.

**LE:** Do you have any specific suggestions for rooting out the corruption in the industry?

**Dr. Moss:** Open up the clinical-trial system. At the present time, as few as **41%** of adult cancer patients even qualify for clinical trials and fewer than **5%** participate. This means that patients in the general population cannot be sure that the results of clinical trials apply to them. By eliminating restrictive admission criteria, the number of potential participants could be greatly increased.

Use overall survival as the main endpoint. Progression-free survival and objective response rates may be useful surrogate endpoints in early stage or exploratory trials. But surrogate endpoints are an insufficient basis for the approval of new cancer drugs. Trials should be

patient-centered and should therefore focus on real benefits.

Withdraw approval of unproven drugs. The FDA should withdraw approval from any drug that has not been proven to actually help people live longer or better. This can be done, as former Commissioner Margaret Hamburg, MD, showed in the case of Avastin for breast cancer. There should be a housecleaning of unproven drugs by the FDA.

End drug industry corruption of the clinical-trial system. Make it illegal for the pharmaceutical industry to offer money to any doctor involved in a clinical trial. Anyone found hiding such payments should be barred from participating in future clinical trials and face criminal charges.

**LE:** The truth about cancer treatments seems pretty grim.

**Dr. Moss:** It is not my intention to discourage cancer patients from seeking effective treatments, but I also cannot be silent about Big Pharma's corruption of the oncology profession. Patients and caregivers deserve recommendations that are based on unimpeachable science, and not on research that has been compromised by the shady practices of giant drug companies.

As a patient myself, who has faced life-threatening cancer, I know that hope and morale are very important to one's peace of mind, and possibly to one's recovery as well.

In fact, four years ago, when my highly skilled and dedicated doctors were actively battling my cancer with me, the last thing I wanted to hear was anything negative about my treatment choices. But this story needs to be told.

I sincerely believe that we will never reach that universally desired "world without cancer" unless we root out the corruption that has overtaken much of the leadership of the oncology profession.

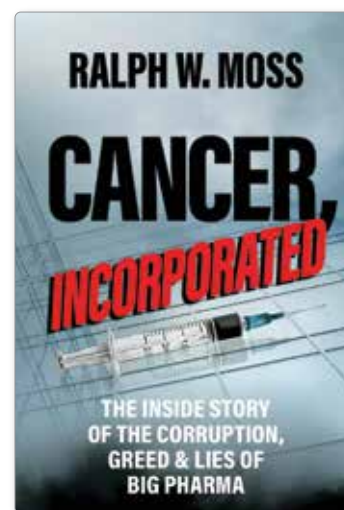
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Dr. Ralph W. Moss has been writing about cancer treatments and the cancer industry since 1974. He is the author of 12 books and four film documentaries on cancer-related topics. Dr. Moss produces 'Moss Reports.' These 500+ page documents offer unbiased, up-to-date, and in-depth analysis of conventional, alternative, and complementary cancer treatments.

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# Onions

BY LAURIE MATHENA



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Chopped onions are notorious for making your eyes water. But their health benefits are nothing to cry over.

A member of the *allium* family of vegetables (which also includes garlic and leeks), onions have important **antiviral** and **immune-boosting** properties.

They are a good source of sulfur, which is important for **detoxification** and **protein synthesis**.

Onions also contain compounds that help support heart health, reduce the risk of certain cancers, and can even improve bone density.

## Heart Health

Studies have shown that onions improve numerous factors associated with heart health.

Red onions in particular contain anthocyanins, which give them their deep red color. People who consume high amounts of anthocyanins have a lower risk of heart attacks.<sup>1</sup>

Onions also contain small amounts of a beneficial flavonoid called **quercetin**.

Animal studies have indicated that consuming onions can reduce heart disease risk factors like inflammation,<sup>2</sup> high triglycerides,<sup>3</sup> and blood clot formation.<sup>4</sup>

## Cancer Prevention

A meta-analysis that included 16 studies and more than 13,000 people showed that compared to those with the lowest intake, people with the highest intake of onions had a reduced risk of **colorectal cancer**.<sup>5</sup>

Another meta-analysis showed that people who consumed the most allium vegetables (like onions and garlic) were less likely to be diagnosed with **stomach cancer**, compared to those with the lowest intake.<sup>6</sup>

This cancer protection is likely due to onions' **sulfur-containing compounds** (which have been shown to decrease the growth and spread of tumors in test tube studies<sup>7</sup>) and flavonoids like **quercetin**<sup>8</sup> and **fisetin**<sup>9</sup> (which may inhibit tumor growth).

## Boost Bone Density

Consuming onions could possibly help prevent osteoporosis by decreasing bone loss and boosting bone mineral density.

In one study of perimenopausal and postmenopausal women, those who ate onions at least once a day had **greater bone density** than those who only ate them once a month or less. And compared to women who never ate onions, those who ate them most frequently decreased their risk of bone fracture.<sup>10</sup>

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*L. rhamnosus* CRL1505 is so effective that it is given to over 300,000 Argentinian school children every year.<sup>2,3</sup> FLORASSIST® Immune & Nasal Defense: be ready for whatever the world has for you.

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2. *Int J Biotechnol Wellness Industr*. 2012; 1:189-198.
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# 45 times Greater Bioavailability Curcumin



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

**Item #02407**

500 mg, 60 vegetarian capsules



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

**Item #02324**

500 mg curcumin + gingerol, 30 softgels



These products are available at fine health food stores everywhere.

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A human study published in **January 2020** showed remarkable systemic benefits when **pro-resolving mediators** were added to **fish oil**.



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Clinical trials show that **vitamin D** decreases rates and severity of **viral respiratory tract** infections. More than **70%** of Americans have either deficient or insufficient vitamin D blood levels.



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Scientists have identified four **plant-based** compounds that support the body's **endocannabinoid** system *without* CBD.



### 46 PREBIOTICS FOR BETTER HEALTH

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Scientists have identified a **probiotic** and **yeast fermentate** combination that **reduced** the frequency of colds and flus by **55%**.