Remarkable Increases in BONE DENSITY

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A patented extract from turmeric root that provides 45 times greater free curcuminoid bioavailability than standardized turmeric powder. (1 capsule daily.)

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ConsumerLab conducted the survey, but it was Consumers who ranked us #1.

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ON THE COVER
HIGH-DOSE VITAMIN K2 BUILDS NEW BONE

Physicians in Japan have prescribed high-dose vitamin K2 to treat osteoporosis for decades.

Human trials show that 45,000 micrograms (45 mg) of vitamin K2 daily increases bone density and reduces fracture risk.

High-dose vitamin K2 is now available without a prescription.

“I WAS NOT SURPRISED TO HAVE OSTEOPENIA”
(William Faloon 2019)

Aging is almost always accompanied by bone loss. Fractures caused by osteoporosis are a leading cause of disability and mortality. Bill Faloon reports on his diagnosis.

THWART POST-MEAL BLOATING AND INDIGESTION

Up to 30% of people complain of after-meal bloating and related discomforts. Researchers have identified plant compounds that target the underlying causes. Clinical studies show they can help prevent gastrointestinal distress.

FISETIN: A LONGEVITY SENOLYTIC

The plant extract fisetin increased lifespan by 10% even when fed to rodents the equivalent of 75 human years. Fisetin counteracts aging via several mechanisms including functioning as a potent senolytic. A new patented green technology increases the bioavailability of fisetin 25 times higher.

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Osteopenia is diagnosed when your bones are weaker than normal, but not so much that they easily fracture.

As I neared age 65, I knew it was time to check my bone density, since aging is almost always accompanied by significant bone loss.

When my results came back as mild osteopenia I was not surprised.

My low-calorie diet contained little calcium and the last supplement I took each day was calcium, so I seldom got to it before the day ended.

I’m grateful to have found out in time to take corrective actions to rebuild skeletal density.

Prevalence of Osteopenia

Bone fractures caused by osteoporosis are a leading cause of disability and mortality in the elderly. Yet a surprising number of younger individuals have osteopenia, which can lead to osteoporosis.

A study published in 2019 found more than 25% of men and women between age 35-50 years already had osteopenia (weakened bones).

As these people age past 50, they are likely to be at risk of more severe bone loss, a condition called osteoporosis, which means fractures become much more likely. With advancing age, adverse outcomes resulting from fractures are common.

Inability to walk following a hip fracture may lead to pneumonia, deadly blood clots, and muscle loss, ultimately increasing the risk of premature death.

Osteoporosis Epidemic

One of every five men over age 50 will suffer an osteoporotic fracture.

One out of every three women over age 50 will suffer a fracture related to osteoporosis.

Having osteoporosis not only increases the risk of fractures, it is also associated with accelerated aging and with an increased risk of:

1. Cancer
2. Cardiovascular disease
3. Dementia

Health-conscious individuals take steps to protect against heart disease, cancer, and Alzheimer’s by taking supplements including CoQ10, fish oil, vitamin D, and others. Often overlooked are nutrients needed for comprehensive skeletal support, like vitamin K.
**Drugs That Improve Bone Density**

A class of drugs called **bisphosphonates**, (that include Fosamax® and Actonel®) help rebuild **bone density**.

There are concerns, however, with short- and long-term use of these drugs in many patients.

Side effects include bone, joint, or muscle pain.13

For oral bisphosphonate tablets, side effects may include nausea, difficulty swallowing, heartburn, irritation of the esophagus, and gastric ulcer.13

These drugs reduce osteoporotic fractures involving the hips and spine in older patients, especially women ages 65 to 80 years with osteoporosis.14

The problem with bisphosphonates is that they focus on limiting additional bone loss, rather than **building** more bone.

Longer-term use of bisphosphonates beyond five years has been linked to increased risk of **atypical fractures** of the femur and **osteonecrosis** of the jaw.13 Some trials, but not others, have also reported increased rates of **atrial fibrillation**.15,16

Better and safer methods of **rebuilding bone** mass are clearly needed.

**High-Dose Vitamin K2 Restores Bone Mass**

The **Japanese** approved *coenzyme Q10* as a heart medication in 1974.

Americans did not gain access to CoQ10 until **1983**.

Analogous to **CoQ10**, the **Japanese** approved a high-dose **vitamin K2** drug in the **1990s** to restore **bone mass** and prevent **fractures**.

**Vitamin K2** supports **new bone formation** and also protects against excess removal of older, but still structurally important bone.17,18

Japanese doctors took a common form of vitamin K2 called MK4 and studied it at the **high dose** of **45 mg** a day.19,20 This is about **15 times more** than what **Life Extension®** supporters supplement with.

The results from studies dating back decades reveal **improvements in bone density** and **reductions in fracture rates**.19-27

**Vitamin K2** **activates** a protein called **osteocalcin** in **bone** that binds **calcium**. If this calcium-binding protein is **not** activated, then natural bone **restoration** may not be possible.

Just as important, **vitamin K2** **activates** a protein in **arteries** and **heart valves** that **shields** them from deadly **calcification**.

**Bone Loss Risk Factors**

There are many reasons for **loss** of bone mass. Many have a false sense of security about their ability to maintain healthy bones, because they avoided some common bone loss risks.

Some of the major controllable or acquired factors that accelerate **bone loss** include:10-12

- Smoking cigarettes
- Excess alcohol ingestion
- Hormone deficits (estrogen, progesterone, testosterone, DHEA)
- Lack of weight-bearing exercise
- Drugs (proton-pump inhibitors, corticosteroids, warfarin, and others)
- Nutrient deficiencies (magnesium, boron, vitamins D & K, calcium)

Add to the above list risk factors such as ethnicity, small body frame, family history, and certain medical conditions.10-12

With so many pathologies impairing one’s ability to maintain healthy bone strength, it becomes clear why **preservation of bone density** requires aggressive measures.

I fear most people look at **osteoporosis risk factors** and think they are avoiding most of them, such as not smoking or taking bone-depleting drugs.

The reality is that virtually **all** these factors might need to be addressed to protect against **osteopenia** and **osteoporosis**.
Remarkable Improvement in Bone Density

Vitamin K2 is critical for calcium to bind to bone to provide structural support.

Clinical trials show that a 45 mg dose of vitamin K2 (MK4) can prevent, or in some cases reverse age-associated bone density loss, and reduce fracture risk.19-27

In one clinical study, researchers divided women in their mid to late 60s with osteoporosis into one of two groups:26

150 mg a day of elemental calcium
or
150 mg of elemental calcium + 45 mg of MK4

As seen in the graph above, lumbar bone mineral density decreased steadily at every time point in the calcium-only group. By the 24-month measurement, the low-dose-calcium-only group lost 3.3% of their bone density!

Impressively, the calcium + vitamin K2 (MK4) group lost little if any bone mass over that same period.26

This study demonstrated how high-dose vitamin K2 added to a modest-dose (150 mg/day) calcium supplement prevented the loss of lumbar spine mineral density over a period of two years. And these are only two of several nutrients needed to maintain bone mass.

Reduction in Fracture Incidence

In this same study,26 the group receiving calcium + high-dose K2 saw a reduction in fracture incidence. The group receiving calcium alone sustained 35 fractures, compared to only 14 fractures in the vitamin K2 + calcium treatment group (see table below.)

As it relates to percentages, patients in the calcium + high-dose K2 group had a significantly lower fracture rate at 15.4% compared to the calcium alone at 35.4%.

This study corroborates the elevated fracture rate observed in women over age 50.

Even more robust results in the calcium + K2 group may have been seen if higher dose calcium, along with vitamin D and other bone nutrients, had been included.
Combining Vitamin D + Vitamin K2

Another study evaluated the effect of vitamin D3 + high-dose K2 in osteoporotic postmenopausal women.27 All the women were encouraged to obtain 1,000 mg of calcium a day plus 400 IU of vitamin D through their food.

After two years, study participants showed the following percent changes in lumbar spine bone mineral density (BMD) compared to baseline:27

- **Calcium group** (calcium lactate 2,000 mg/day) — 0.79% reduction in BMD
- **Vitamin D3 group** (30 IU/day) — 0.38% increase in BMD
- **Vitamin K2** (45 mg/day) — 0.90% increase in BMD
- **Vitamin K2 + D3 group** — 1.35% increase in BMD

These data reveal the benefits of combined bone-building nutrient supplementation.

New Recommendation to Restore Bone Structure

Most of us have lost more bone than we realize. Nutrient formulas containing calcium, magnesium, vitamins D and K, proper hormone balance and healthy lifestyle choices are all important in slowing bone loss and partially reversing it.

Most of us over age 50 should now consider a strategy based on three decades of human studies emanating mostly from Japan. This has demonstrated meaningful bone density improvements and marked reduction in fracture incidence.

Consider a supplement that provides approximately:

- 45 mg of vitamin K2 (MK4)
- 700 mg of calcium*
- 1,000 IU of vitamin D3
  (plus nutrients like magnesium and boron)

Many readers obtain additional vitamin D3, zinc, boron, and magnesium from their nutrient formulas.

Those who take this new approach to restoring lost bone mass may not require any other vitamin K supplement. That is because this 45 mg potency of vitamin K2 is likely to provide superior protection against calcification of arteries, soft tissues, and heart valves, along with restoration of bone mass.

Conclusion

The magnitude and prevalence of age-related bone loss is underappreciated.

Osteopenia and osteoporosis are worsened by poor lifestyle choices (like excess alcohol) and drugs like stomach-acid blocking drugs that impede calcium absorption.

If high-dose vitamin K2 is widely adopted in the United States, it could reverse the surging epidemic of bone loss and crippling fractures occurring in men and women over age 50.

This is of even greater importance to people like myself who intentionally reduce their overall calorie intake, and thus ingest less dietary calcium.

In this special edition, you’ll learn how easy it is to boost your vitamin K2 intake.

For longer life,

William Faloon
Note to Warfarin (Coumadin®) Users

Human studies validate the safety of high-dose vitamin K2 (MK4) in people not taking warfarin. Warfarin is a powerful anti-coagulant drug that functions as a vitamin K antagonist.

Warfarin users are told to avoid vitamin K foods and supplements. A side effect of warfarin is accelerated bone loss caused by lack of vitamin K.

If you are using warfarin, consider asking your doctor about newer anti-coagulant drugs (Pradaxa®, Eliquis®, Xarelto®) that do not function by antagonizing vitamin K.

Use of these newer anti-coagulant drugs can enable you to benefit with vitamin K and still obtain needed anti-coagulant effects.

References

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Thwart POST-MEAL Bloating and Indigestion

BY MICHAEL DOWNEY
As people age, they often experience bloating, gas, or nausea before they even finish a meal.

It’s more common than most people realize.

Up to 30% of people suffer from after-meal **bloating**, that uncomfortable feeling that your belly is swollen.1-3

Even when small meals are consumed, after-meal **bloating** remains a widespread problem.

Scientists have identified four **plant extracts** that target **underlying causes** of gastrointestinal discomforts.

In one human trial, more than 63% of the subjects taking an **artichoke-ginger** blend experienced significantly reduced feelings of bloating, gassiness, nausea, and other symptoms of indigestion.4

A **fennel-curcumin combination** relieved symptoms of **irritable bowel syndrome**, including bloating and stomach pain, by more than 50%, and **completely prevented all symptoms** in 25.9% of users.5

Taken together, these nutrients promise to relieve post-meal distress and improve quality of life.
The Causes of Bloating

**Bloating** is one of the most commonly reported gastrointestinal symptoms. It’s characterized by a feeling of excessive fullness, trapped gas, distension, and abdominal pressure and pain.²

No treatment has proven consistently effective,² and drugs may have serious side effects. **Propulsid** was a drug frequently prescribed to alleviate bloating. But it caused abdominal pain, indigestion, gas, and nausea.⁶ It was removed from the U.S. market after it was associated with heart rhythm abnormalities.⁷

Two of the underlying causes of after-meal bloating are slow **gastric motility** and excess **gas production**.

When gastric motility slows, the ability of the stomach muscles to move food through the digestive tract is impaired.

Artichoke and Ginger

**Indigestion** in the upper abdominal region is described as bloating or gassiness, a burning sensation, nausea, or feeling too full too quickly after starting to eat.

About 40% of patients have abnormally **delayed gastric emptying**, which means food simply sits in the stomach longer than it should.

**Prokinetic** drugs accelerate gastric emptying. They are often used to treat indigestion. But like Propulsid, they have side effects.⁸

Fortunately, there are specific **nutrients** used for centuries that safely facilitate **gastric emptying**.

Researchers first focused on **artichoke leaf** and **ginger root**, which have long been used in traditional medicine to treat indigestion.⁸-¹⁰

**Ginger** has been shown in animal and human studies to promote **gastric motility**.⁴,⁸,¹⁰

**Artichoke** promotes **bile acid secretion** from the liver. Bile acid secretion is essential for accelerating gastrointestinal transit.

Artichoke is also an **antispasmodic**, which means it suppresses gut spasms or cramping. This also helps speed the movement of food through the digestive tract.⁴,⁸,¹⁰

Scientists decided to combine ginger and artichoke extracts to test their effects on bloating.⁴,¹¹

**Human Trials**

Researchers created a blend of 100 mg of artichoke leaf extract and 20 mg of ginger root extract.⁴,¹¹

They tested it on 126 healthy men and women, aged 18-70, who had **functional dyspepsia** (indigestion). This was defined as having had complaints of early satiety (fullness), postprandial fullness (feeling too full after eating), bloating, or nausea for at least three months during the last year, without a known structural or biochemical cause.⁴

In a randomized, double-blind, placebo-controlled study, two groups took either 120 mg of the artichoke-ginger blend or a placebo twice daily. Patients rated the severity of each of six dyspeptic symptoms: fullness, bloating, early satiety, nausea, vomiting, and upper abdominal pain.

In 14 days, 44.6% of participants taking the artichoke-ginger blend had a marked (clinically significant) improvement in digestive symptoms, compared to 13.1% of the placebo users.

After four weeks, 63.1% of the artichoke-ginger group had a marked symptom improvement, while only 24.6% showed improvement in the placebo group. No adverse effects were reported.⁴

In another study, scientists used ultrasound to measure the size of the stomach area of 11 healthy men and women, aged 20-60, both before and after a standardized meal.¹¹

When the artichoke-ginger blend was taken, subjects had a significantly smaller stomach area than when the placebo was taken. This indicates that the artichoke-ginger blend works by encouraging enhanced gastric emptying.¹¹
Fennel Seed and Curcumin Relieve Pain and Gas

Two other nutrients have been used to aid digestion: fennel and curcumin.

Seeds from fennel, a plant known for its licorice flavor, have long been consumed after meals to promote digestion and prevent flatulence.\(^{12}\)

Studies show that fennel reduces gas production by inhibiting the activity of a methane-producing bacterial enzyme.\(^{13}\)

In addition, clinical trials have shown that fennel seeds, tea, and seed oil promote gastrointestinal stimulation, improving gastric motility.\(^{5,14,15}\)

Like artichoke, fennel also has an antispasmodic effect, reducing irregular muscle contractions that impair normal gut motility.\(^{5}\)

Researchers combined fennel seed oil and a low-dose curcumin in a clinical trial to test their effect on bloating and abdominal pain.\(^{5}\)

Clinically Effective

Scientists enlisted 121 male and female volunteers, aged 18-60, who suffered from irritable bowel syndrome (IBS) for a randomized, double-blind, placebo-controlled trial.\(^{5}\) IBS is a chronic disorder characterized by abdominal pain, bloating, and abnormal bowel movements in the absence of identifiable cause.

Participants took a capsule twice daily that contained either a placebo or a combination of 25 mg of fennel seed oil and 42 mg of curcumin.

WHAT YOU NEED TO KNOW

Relief for Post-Meal Problems

- **Bloating** is one of the most common gastrointestinal symptoms, marked by a feeling of excessive fullness, gas, and abdominal pressure and pain.

- Scientists have identified **four clinically effective** compounds that target the underlying causes of bloating before it occurs.

- A blend of artichoke leaf and ginger root extracts relieves symptoms of dyspepsia (indigestion), including bloating, nausea, vomiting, and upper abdominal pain.

- A mix of fennel seed oil and curcumin decreases bloating, abdominal pain, and other severe symptoms of irritable bowel syndrome.

- Taken together, ginger root, artichoke leaf, fennel seed oil, and curcumin may help prevent or significantly reduce gastrointestinal distress, and improve quality of life.
Researchers combined low-dose curcumin with fennel seed oil to reduce assorted symptoms of bloating. The curcumin was added to reduce inflammation in the gut. Fennel seed oil was used for its antispasmodic properties.

When these two compounds were used together, researchers found reduced abdominal pain and abdominal distention in study subjects.

After 30 days, those taking the fennel-curcumin mix reported an average 50.05% decrease in bloating, abdominal pain, and other IBS symptoms, nearly double the 26.12% decrease in the placebo group. All symptoms were improved by treatment. Among those taking the fennel-curcumin mix, 25.9% became completely symptom-free, compared to 6.8% of placebo users.

The treated group also reported significant improvement in quality of life, with no adverse effects.

Taken together with ginger root and artichoke leaf, this fennel-curcumin combination may significantly improve or even prevent after-meal bloating, gas, and abdominal pain, providing a solution to a problem many people thought they just had to live with.

**Summary**

Up to 30% of people complain of bloating after eating, which is often accompanied by gas, abdominal pressure and pain, and reduced quality of life.

Scientists have identified four compounds that target the underlying causes of this discomfort, which are slow gastrointestinal motility (movement) and excess gas production.

Ginger root, artichoke leaf, fennel seed oil, and curcumin have been shown to target these causes.

In clinical trials, they significantly reduce bloating, gas, feelings of excessive fullness, stomach distension, abdominal pain and discomfort.

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

**References**

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DIGESTIVE UPSETS?

Bloat Relief helps relieve occasional discomfort, such as gas and bloating following a meal.

Scientists have combined four plant extracts that target underlying causes of gastrointestinal discomforts:

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- Artichoke leaf
- Fennel seed oil
- Curcumin

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High-Dose VITAMIN K2 Builds New Bone

BY STEPHEN ROSS
With age, our bones get thinner and weaker. This leads to increased fractures that are leading causes of disability as people age past 50 years.\(^1\)

The numbers are chilling. Within a year of suffering a hip fracture, up to 20\% of patients will die.\(^1\) And almost any kind of broken bone increases the risk of death in older people.\(^2\)

Physicians in J apan discovered a way to help prevent bone loss and protect against fractures.

For more than two decades they have been prescribing a high-dose vitamin K2 in the form of menaquinone-4 or MK4.\(^3\)

This high-dose vitamin K, used as a prescription drug in J apan, is now available as a dietary supplement.

Vitamin K is found in small amounts in many foods and over-the-counter formulas. But at the high dose of 45 mg, it has a profound impact, helping to:\(^4-11\)

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

In a two-year study on older people with osteoporosis, high-dose vitamin K2 cut the number suffering a vertebral fracture by half.\(^11\)

Along with other nutrients known to support bone strength, vitamin K2 plays an essential role in maintaining and helping to restore bone density.
What Causes Bone Loss?
To maintain structure, old bone is constantly being broken down, and new bone is being built up.
For the first decades of life, bone density (how tightly bones are packed with minerals) increases. Peak bone density and bone strength then plateau for about two decades.
By age 40, bone density starts to fall and continues to decline into old age. In women, the speed of bone loss accelerates with the onset of menopause.
That drop in bone-mineral density leads to a reduction in bone strength. Bones become brittle and prone to fractures, even from minor injuries (or stress fractures that occur during normal use).
The early stage of bones weakening is called osteopenia.
As bone density continues to drop, osteoporosis develops, which means “bone full of pores or holes.”
Most people don’t know they have osteopenia or osteoporosis until it’s too late—when they suffer a fracture.

High Doses of Vitamin K2
The encouraging news is there is something we can do about age-related bone loss and risk of fractures.
Vitamin K2 has been used to treat osteoporosis in Japan for decades.³
Research has confirmed that this specific form of vitamin K is critical for bone health and other aspects of healthy aging.
In low doses (60 mcg), vitamin K promotes normal blood clotting. This small amount of vitamin K is normally obtained from dietary sources.
Beginning in 1999, scientists at Life Extension® recognized that higher doses of vitamin K can better keep calcium in bones and help prevent calcification of soft tissues such as heart valves, arteries, and brain cells.
As data accumulated over the past 21 years, the suggested daily dose of vitamin K steadily increased to over 2,000 mcg, which is far higher than the tiny amount needed for normal blood coagulation.

Vitamin K2 Safety Profile
What’s interesting is how vitamin K functions to enable normal coagulation.
Once low doses activate coagulation proteins in the liver, then no matter how much more vitamin K is ingested, there is no excess coagulation/clotting risk. That’s because when coagulation proteins are fully saturated with vitamin K, they cannot take up more vitamin K to cause greater coagulation potential.
With this understanding, the opportunity to use far higher vitamin K doses to build strong bones became an enticing reality.
So much so that Japanese doctors began prescribing 45,000 mcg of vitamin K2 and have verified profound improvements in bone health in older adults.³

Building New Bone
Bone density is influenced by two types of bone cells: osteoclasts and osteoblasts.
Osteoclasts break down old bone. Osteoblasts build new bone.
Healthy bone relies on a balance of activity between these two types of cells. They constantly remodel bone structure while keeping bone density stable.
As we age, this balance is lost. Osteoclast activity outweighs osteoblast activity. As a result, bone is broken down faster than new bone can be built up. As bone density drops, osteopenia and osteoporosis manifest.
Vitamin K2 appears to restore healthy balance. In preclinical studies, it promotes an increase in bone-building osteoblast activity and reduces osteoclast activity.\textsuperscript{12,13} With this balance restored, more bone is built, less is destroyed, and bone mineral density is maintained or even increased.

In addition, in order to lay down new bone, osteoblasts need a protein called osteocalcin. This protein binds to calcium, helping osteoblasts turn calcium into healthy new bone.\textsuperscript{13} Vitamin K2 helps convert osteocalcin into its active form.\textsuperscript{13,14}

**WHAT YOU NEED TO KNOW**

**Prevent Fractures with Vitamin K2**

- Bone loss begins to occur in our 40s and progresses with advancing age.
- This weakening of bone can lead to osteoporosis and greatly increased risk of fractures, which can cause disability and dramatically increase risk of death.
- High-dose vitamin K2 has been used as a treatment for osteoporosis in Japan for decades.
- Vitamin K2 acts by several mechanisms to improve bone health in preclinical studies, including restoring balance to the process of bone breakdown and formation.
- Human trials have shown that daily intake of 45 mg (45,000 micrograms) of vitamin K2 maintains or increases bone density and reduces the risk of fractures.
- Other nutrients, including calcium and vitamin D3, also support bone health and help maximize vitamin K2’s benefits.
Keeping Bones Strong

Human trials have tested the benefits of vitamin K2 on bone health.\textsuperscript{4-11} The results show that high-dose vitamin K2:

- Increases active osteocalcin levels required for new bone formation, and
- Maintains or increases bone mineral density.

Many of these studies have been performed in older people with osteoporosis. Even those already at this advanced level of bone loss benefit from oral vitamin K2.

One example comes from researchers in Japan.\textsuperscript{11} They enrolled older individuals in a study who all had a diagnosis of osteoporosis. Patients were randomized to receive either calcium alone or calcium plus 45 mg of vitamin K2 daily.

Over the course of the two-year study, subjects who received only calcium continued to lose bone density, dropping by about 3%.

A 10% drop in bone density more than doubles the risk for fractures of the vertebra (the bones making up the spine) and hip.\textsuperscript{15} This means that those treated only with calcium in this study (who lost 3% of bone density) increased their risk of fracture.

Vitamin K2 and Bisphosphonates

The bisphosphonates are a group of drugs prescribed to slow bone loss in osteoporosis. They include medications such as alendronate, risedronate, and others.

Research shows that vitamin K2 does not interfere with bisphosphonates and can safely be used at the same time. There are even some data to suggest that they may have an additive effect, protecting bone density better together than either one alone.\textsuperscript{28}

On the other hand, people receiving high-dose vitamin K2 in addition to calcium largely maintained their bone mineral density. They also benefited from a significant increase in levels of active osteocalcin.

Reducing Fracture Risk

The scale of osteoporosis and related fractures is staggering.

Worldwide, as many as one-third of women and one-fifth of men over age 50 will suffer an osteoporotic fracture.\textsuperscript{1} And after suffering one fracture, the risk of future fractures increases by a whopping 86%.\textsuperscript{1}

Fractures of the hip and vertebra in particular are associated with pain, loss of mobility, and risk of death.\textsuperscript{1} For example, people who suffer a vertebral fracture have an 8-fold increase in mortality compared to other individuals their age.\textsuperscript{1}

In the Japanese study on older people with osteoporosis, 30% of those receiving only calcium suffered vertebral fractures during the two years of the study. But only 14% of those also receiving high-dose vitamin K2 + calcium had a vertebral fracture.\textsuperscript{11} (These study subjects did not receive supplements like vitamin D and magnesium, also needed to protect aging bones.)

Another Japanese clinical trial found that 45 mg of vitamin K2 daily maintained bone mineral density and reduced the risk of fractures.\textsuperscript{6}
Nutrients That Work with Vitamin K2

As in all aspects of health, no one nutrient is enough on its own. Vitamin K works with other nutrients to form healthy bone. The following nutrients have been shown to keep bone-density levels up and to maximize the benefits of vitamin K2:

• Calcium is the major mineral that forms the hard, strong matrix of bone. Adequate calcium is needed so that osteoblasts have it readily available to build bone tissue.

• Vitamin D helps absorb calcium from the gut after a meal and stimulate the production of the protein osteocalcin, needed to form new bone.14

• Magnesium, like calcium, makes up the mineral matrix of bone. Adequate levels are needed to maintain healthy bone density.16

• Zinc, Manganese, Silicon, and Boron. These minerals have been shown to be important for optimal bone formation and health. Low intake of each of these minerals is associated with bone loss, and increased intake improves bone health in animal models and in humans.17-27

Taken together with high doses of vitamin K2, these nutrients protect against bone loss and fractures.

Summary

As our bones become thinner and weaker with age, the risk of dangerous and life-threatening fractures increases.

High-dose vitamin K2 has been used to treat the bone disease osteoporosis for decades in Japan. Clinical trials demonstrate that daily intake of 45 mg of vitamin K2 maintains or increases bone-mineral density and reduces the risk of fractures.

Along with other vitamins and minerals crucial for bone health, vitamin K2 is a powerful tool to help build stronger, healthier bones well into old age.

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

Cardiovascular Disease Benefits

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

However, in soft tissues, calcification can be extremely dangerous. In blood vessels, it leads to the buildup of atherosclerotic plaques associated with cardiovascular disease.29,30 This occurs because it activates matrix Gla protein, which inhibits calcification of blood vessels.

For this reason, vitamin K2 may be protective against cardiovascular disease.31

In addition, while vitamin K1 is used to help blood clot in response to blood vessel injury, vitamin K2 has not shown any impact on clotting or coagulation.32 Still, anyone taking warfarin, a powerful anticoagulant, should consult a physician before deciding to take any form of vitamin K.
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MacuGuard® Ocular Support provides:

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

References


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**SUPER SALE PRICE**

<table>
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<th>Item #01993</th>
<th>60 softgels</th>
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<td>$29.70</td>
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<td>4 bottles</td>
<td>$27 each</td>
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Each bottle lasts for two months.

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• Improve bone density

New high-potency Mega Vitamin K2 provides 45,000 mcg of MK-4 in a one capsule daily serving.

Mega Vitamin K2 is a perfect complement for those taking supplements like Bone Restore. A new formula providing 45,000 mcg of MK4 plus highly absorbable calcium and other skeletal-support nutrients called Bone Restore Elite can be viewed by turning this page. Those choosing Bone Restore Elite do not need to take Mega Vitamin K2 as each product provides a high potency (45,000 mcg) of vitamin K2.

For full product description and to order Mega Vitamin K2, call 1-800-544-4440 or visit www.LifeExtension.com

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Neuro-Mag® Magnesium L-Threonate was specifically formulated by MIT scientists to be uniquely absorbable by brain and nerve cells. The numbers of synapses that connect brain cells decline with aging. Magnesium L-Threonate has been shown to improve synaptic density and other structural components of the brain.*

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For full product description and to order Neuro-Mag® Magnesium L-Threonate or Neuro-Mag® Magnesium L-Threonate Powder, call 1-800-544-4440 or visit www.LifeExtension.com

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**Bone Restore Elite** is designed to help maintain optimal **bone density**. The formula provides **high** potency **vitamin K2** (MK4) used in **clinical** trials along with proven skeletal-strengthening nutrients.

Each serving provides:
- **45,000 mcg** of **vitamin K2 (MK4)**
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- **1,000 IU** of **vitamin D3**
- **Key minerals:** **magnesium, boron, zinc, silicon, and manganese**

**High potency for strong bones.**

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**CAUTION:** If you are taking Warfarin (Coumadin®) or related medications, consult your healthcare practitioner before taking this product.


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**SUPER SALE PRICE**

**Item #02416** • **120 capsules**

- **1 bottle** $31.05 • **4 bottles** $28.35 each

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FISETIN: A Longevity Senolytic

BY ZACH WHITE
For decades, scientists have searched for compounds that can slow degenerative aging processes.

A recent focus is a plant extract called fisetin.

Found in strawberries, apples, and other plants, fisetin has a range of benefits that may increase longevity.1,2

Fisetin has been shown to:

- Function as a senolytic, clearing away dysfunctional senescent cells and allowing healthy cells to thrive,3
- Protect the brain in various models of neurodegenerative disorders,2,4-9
- Improve outcomes in people who have suffered strokes,10
- Help prevent malignant changes in cells,11-14 and
- Help fight obesity and type II diabetes.15-17

Several human trials are currently underway.

The challenge up until now was that fisetin is converted to an inactive form in the digestive tract. This means very little is absorbed into the blood stream.

For the first time, scientists have developed a low-cost method to increase absorption up to 25 times higher,18 thus enabling fisetin to be distributed throughout the body.
What Is Fisetin?

Fisetin, a flavonoid, is found in various fruits and vegetables including strawberries, apples, persimmons, grapes, and onions.

Its benefits overlap with some other flavonoids, including green tea catechins and quercetin. But it has its own unique set of biological properties.

Most notably, a recent study found fisetin to be the most potent senolytic compound among a group of flavonoids that were tested. Senolytics are at the center of today’s anti-aging research.

Fisetin Extends Lifespan

When cells become old or dysfunctional, they’re supposed to die off to make room for new cells. But as we age, many cells become senescent instead.

What this means is that these cells lose their ability to divide or perform basic functions and refuse to die. Some scientists refer to senescent cells as “zombie cells.”

Senescent cells don’t just linger around. They pump out toxic compounds that degrade nearby cells and incite chronic inflammation that causes systemic damage.

Cellular senescence has become a major target for anti-aging research. Preclinical studies indicate that compounds called senolytics remove senescent cells and can slow or even reverse aging processes.

Recent research has found that fisetin is an exceptionally powerful senolytic. When compared to other plant compounds, including quercetin, fisetin was the most effective at removing senescent cells, both in cell culture and in mice.

The effects are dramatic. Mice given fisetin lived an average of about 2.5 months longer, an almost 10% extension of lifespan—even when treatment was started at the human equivalent of 75 years of age.

The Mayo Clinic has begun clinical trials to study the ability of fisetin to reduce senescent cell burden in aging humans.

Anti-Aging Properties

Sirtuin proteins are another anti-aging target. These cellular protectors are found in all cells in the body, and are vital for keeping cells performing at peak level.

Sirtuin function tends to diminish with age. But fisetin activates sirtuin function in cells, countering this decline. In various animal models, sirtuin activation has been shown to extend lifespan significantly.

Fisetin may protect against aging in other ways:

- It reduces inflammation, a driver of many chronic illnesses and even of aging itself.
- It mimics some of the effects of a calorie-restricted diet, which has been shown to boost resistance to disease and increase lifespan.
- It helps prevent oxidative damage that leads to accelerated aging and degenerative disease.

Longer lifespan in old mice with fisetin supplementation.

Mice given fisetin by itself lived an average of 10% longer even when treatment was started at the human equivalent of 75 years of age.
Preventing Obesity and Diabetes

Obesity leads to a skyrocketing risk of metabolic disorders such as type II diabetes. It also increases the risk for cardiovascular disease, cancer, dementia, and many other disorders.

Preclinical studies show that fisetin appears to act as a kind of “metabolism control switch,” reducing fat cell accumulation and suppressing activation of the protein mTOR, which is linked to weight gain. In mice fed a high-fat diet, fisetin prevented increase in body weight and accumulation of harmful white fat tissue.15

Fisetin also helped fight fat accumulation in the livers of animals fed a high-fat diet, a common occurrence with metabolic disease that can compromise liver function and lead to fatty liver disease.35-38

WHAT YOU NEED TO KNOW

Fisetin Promotes Healthy Longevity

- **Fisetin** is a compound found in several fruits and vegetables, including strawberries, apples, grapes, and onions.

- Fisetin is the **most potent senolytic compound** found among a panel of flavonoids, selectively removing senescent cells and extending longevity in animal studies.

- This flavonoid has also been shown in preclinical studies to help protect against cancer, type II diabetes, and obesity, and in a human study to improve outcomes in stroke victims.

- Taken orally, pure fisetin is converted to an inactive form in the body. But scientists have discovered that combining it with galactomannans from fenugreek prevents that from happening.

- A new formulation boosts the bioavailability of fisetin by **25 times**, allowing more of it to circulate throughout the body, promoting health and supporting longevity.
Fisetin may provide benefits for those already suffering from type II diabetes.

In rodent models of diabetes, fisetin lowers body weight and leads to improved glucose control with lower hemoglobin A1c levels, a marker of blood sugar regulation over time.16,17

Poorly controlled diabetes often causes disabling or life-threatening complications throughout the body. In mice, fisetin significantly reduces the severity of diabetic complications, including slowing the progression of cataracts, preventing kidney damage, and improving kidney function.16,39

A human trial of fisetin’s ability to protect kidney function, particularly in diabetes patients, is currently underway.40

**Brain Benefits**

People who suffer from a stroke are often treated with medication to dissolve the clot blocking blood flow to the brain. This can save a patient’s life, prevent damage to the brain, and even reverse the symptoms of stroke in some patients.

But ER doctors are working against the clock when treating acute (ischemic) stroke. The best chances of success occur when treatment begins within three hours of the onset of symptoms.41 Many people suffering a stroke are treated too late and suffer permanent neurological injury (and paralysis).

A recent study shows that combining clot-dissolving medication with fisetin significantly extends the treatment window.10

Patients receiving fisetin in addition to usual treatment up to five hours after a stroke had neurological outcomes as good as those treated within three hours. This extension of the therapeutic window means that many stroke victims who would otherwise suffer permanent loss of brain function have a better chance of recovery.

Fisetin has also shown neuroprotective benefits in animal models of Alzheimer’s disease, Parkinson’s disease, ALS (amyotrophic lateral sclerosis), and other brain pathologies, reducing the severity of disease and improving cognitive function.2,4-9

**Fighting Cancer**

Fisetin has shown potential in preventing cancer and limiting the growth and spread of existing tumors in preclinical studies. Among its anti-cancer properties:

- Fisetin induces apoptosis, or programmed cell death, in cancer, which can facilitate removal of tumor cells.47-50

- As an anti-inflammatory, fisetin reduces compounds that contribute to chronic inflammation and cancer progression.42-45 In a study of patients with colorectal cancer, fisetin reduced levels of pro-inflammatory mediators.46

- Fisetin enhances autophagy,51 cellular housekeeping that keeps cells functioning normally. Enhanced autophagy can inhibit cancer cell survival.

- Fisetin helps prevent angiogenesis, the formation of new blood vessels, in cancer, starving tumor cells of oxygen and glucose.52,53

- Fisetin helps prevent oxidative damage which can contribute to DNA mutations and cancer development.42,43

- Fisetin may inhibit cancer cell migration and metastasis, the spread of cancer to a different part of the body.54
Improved Bioavailability

In its pure form taken orally, there’s a problem with fisetin: Once it reaches the gut, enzymes in the body rapidly modify it into a form which is inactive and all but useless.

Scientists have discovered a way around this problem. By combining it with natural compounds called galactomannans isolated from the herb fenugreek, fisetin is protected from being modified in the intestinal tract. It remains active and can be readily absorbed into the bloodstream.

In a recently conducted study, researchers found that the newly formulated fisetin-galactomannan combination, using a patented green technology, increases bioavailability (how much is absorbed and circulates) in people by 25 times.18

This opens a brand-new door in enabling aging people to derive meaningful benefits by supplementing with a low-cost nutrient.

Summary

Fisetin is a compound found in many plants, including strawberries and apples.

It is the most effective senolytic compared to a panel of flavonoids, removing aged, dysfunctional senescent cells in preclinical studies. This may help improve function in older age, shield against chronic disease, and increase healthy longevity.

In mice, fisetin alone extended lifespan by approximately 10%.

Extensive research also demonstrates the potential of fisetin to help protect against cancer, stroke, obesity, type II diabetes, and other metabolic disorders.

A new fisetin formula compounds it with fenugreek, which protects it from inactivation in the gut. This allows more fisetin to be absorbed and distributed throughout the body for systemic benefits.

(Turn page to review options for using fisetin as a senolytic and to view references.)
If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

References

OPTIONS TO REMOVE SENESCENT CELLS

Most of you are reducing your senescent cell burden by:

• **Two-day-a-week fasting** (not eating 2 days each week) or time-restricted eating (fasting 16-18 hours most days) and/or some other form of dietary restriction,
• Several times a year dosing using **dasatinib + quercetin** and/or,
• Weekly dosing using **black tea theaflavins + quercetin + apigenin**.

**Fisetin** is arguably one of the most focused, targeted senolytic agents, based upon current science. For the first time, people can obtain it in **bioavailable form** as opposed to taking over 1,400 mg a day of fisetin by itself and hoping enough is absorbed into your bloodstream.

For those who want to continue with a **weekly senolytic** program, taking seven capsules once-a-week of **bioavailable fisetin** along with a **black tea theaflavins + quercetin + apigenin** formula is an option.

Alternatively, you may also take the bioavailable **fisetin** dose **daily** for its **other** benefits and continue with weekly **black tea theaflavins + quercetin + apigenin**.

There is potential benefit to daily senolytic as this is how it happens in younger people with strong immune systems that constantly remove senescent cells. 55

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

While the longevity data on **dasatinib** are compelling, some people experience mild flu symptoms or GI upsets, whereas **fisetin** does **not** cause these unpleasant side effects.

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

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**Highlights from Recent Study**

• **Senescent cell production rate increases with age** due to accumulation of mutations, telomere damage, other factors triggering cell senescence.
• **Senescent cells catalyze their own production** by paracrine and bystander effects.
• **Senescent cell** removal decreases with age due to decline in immune surveillance functions.
• **Senescent cells reduce their own removal rate**.


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**Senescent Cell Removal Declines with Aging**

Senescent cells turn over in **five days** in 3-month-old mice but take **25 days** in 22-month-old mice. This model predicts a vicious cycle where senescent cells accumulate faster and are degraded slower.

At the point of **30% senescent cell load** animals often appear to reach tipping point **resulting in death**.

“Our results suggest that treatments that remove senescent cells can therefore have a double benefit: an immediate benefit from a reduced senescent cell load, and a longer term benefit from increased senescent cells removal.”

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

In preclinical studies, fisetin:

- Mimics effects of calorie reduction²
- Targets longevity pathways³⁻⁶
- Extends lifespan of mice by about 10%⁷
- Removes senescent cells through senolytic action⁷
- Suppresses excess mTOR activation⁸

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

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

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

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

References

SUPER SALE PRICE
Item #02414 • 30 vegetarian capsules
1 bottle $10.13 • 4 bottles $9 each

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

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Lutein, trans-zeaxanthin, meso-zeaxanthin, and saffron help maintain structural integrity of the macula and retina. Just one softgel per day.

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Patented turmeric root extract provides 45 times greater free curcuminoid bioavailability plus ginger and broad-spectrum turmerones.

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Superior ubiquinol form of CoQ10 (100 mg) plus shilajit shown to double mitochondrial CoQ10 levels.

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Bone Restore Elite with Super Potent Vitamin K2 • 120 capsules, Item #02416
Helps maintain bone density by combining high potency vitamin K2 (45 mg) with calcium and other skeletal-strengthening nutrients. $31.05 $28.35

NAC (N-Acetyl-Cysteine) • 600 mg, 60 capsules, Item #01534
Supports healthy levels of glutathione for protection against free-radical damage. $9.45 $8.33

Bio-Fisetin • 30 vegetarian capsules • Item #02414
After years of relentless research, an absorbable form of the plant flavonoid fisetin is finally available to target senescent cells. $10.13 $9

Mitochondrial Energy Optimizer with PQQ • 120 vegetarian capsules, Item #01868
Glycation-protection formula helps maintain cellular integrity, and mitochondrial biogenesis. Provides 1,000 mg of carnosine along with R-lipoic acid, taurine, benfotiamine, and PQQ. $45.90 $40.50

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Four plant extracts target underlying causes of gastrointestinal discomforts, such as gas and bloating following a meal. $22.28 $20.25

PQQ Caps • 10 mg, 30 vegetarian capsules, Item #01500
Promotes generation of new mitochondria in aging cells. $12.15 $9.90

Senolytic Activator • 24 vegetarian capsules, Item #02301 (3-month supply)
Highly absorbable forms of quercetin phytosome, black tea theaflavins, plus apigenin designed to help the body to manage senescent cells. $16.20 $14.40

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Protect Your Respiratory Tract During Winter Season

BY ROBERTA STANTON
N-acetyl-L-cysteine is an amino acid derivative that breaks down excess mucus in air passages.

Used by physicians for decades, N-acetyl-L-cysteine has a wide variety of benefits, especially helping to protect the lungs and airways of the respiratory tract.

Known by many as NAC, N-acetyl-L-cysteine has been shown to reduce the number of harmful pathogens, including bacteria and viruses.1-6

Clinical studies have shown that NAC can help treat or prevent worsening of chronic bronchitis and acute respiratory distress syndrome, an often fatal complication in patients with pneumonia or other severe lung infections.7-12

In patients with chronic obstructive pulmonary disease (COPD), N-acetyl-L-cysteine has been associated with lower rates of exacerbations (periods of worsening of symptoms) and fewer days spent in the hospital.4,13-18

Most individuals gain benefits from using 600 mg to 1,800 mg/day in divided dosages.
What Is N-Acetyl-L-Cysteine?

N-acetyl-L-cysteine (NAC) is a precursor of L-cysteine, the amino acid cells need to produce one of the most powerful antioxidants in the body, glutathione.19,20

Found in every cell in the body, glutathione fights the oxidative stress that is closely associated with many age-related chronic diseases.21

But scientists have found that N-acetyl-L-cysteine does much more than this. It also protects the respiratory system from a number of different pathogens and diseases.

Controlling Excess Mucus

Healthy lungs have a built-in cleaning and protection system.

A small amount of mucus is secreted to coat the walls of the airways. This mucus traps inhaled particles, many of which can be irritants, infectious, or worse. Then, tiny projections called cilia on the surface of cells lining the airways sweep away the mucus and trapped particles, keeping airways clear and protecting the lungs from potential pathogens.

Many conditions, from allergies to infection to lung disease, can cause this system to become dysfunctional, leading to the secretion of large amounts of mucus.22

When excess mucus accumulates, it becomes sticky and hard to remove, leading to difficulty breathing. This complicates many lung conditions, including bronchitis, emphysema, asthma, cystic fibrosis, and lung infections.22

Doctors have been using inhaled N-acetyl-L-cysteine to reduce mucus since the 1960s.23 It breaks down mucus secretions, making them less dense and sticky.

N-acetyl-L-cysteine also reduces the thickness of the mucus.3 It does this by reacting with bonds within the mucus proteins and thinning the mucus.4,24

This helps clear the airways and makes it easier for the cilia to sweep away mucus and trapped particles.3

Reducing Oxidative Stress

N-acetyl-L-cysteine is a highly effective precursor to the antioxidant glutathione, which reduces oxidative stress and free-radical tissue damage.3,4,24

Taken orally, NAC is rapidly absorbed and distributed throughout the body, where it provides the building blocks for cells to produce their own glutathione.

N-acetyl-L-cysteine is also a direct antioxidant itself. Even before conversion into glutathione, it scavenges free radicals that could otherwise cause damage.4

Oxidative stress is a common contributor to many disorders of the respiratory system, from infection to chronic obstructive pulmonary disease (COPD), disorders of the lungs that cause difficulty breathing.4

By bolstering antioxidant reserves, and thus reducing oxidative stress, N-acetyl-L-cysteine offers powerful protection to the lungs.
For example, in COPD such as emphysema, oxidative stress in the lungs contributes to inflammation, abnormal constriction of the airways, fluid in the lungs, excess mucus secretion, and other tissue damage. N-acetyl-L-cysteine reduces oxidative stress and the damage it does while also reducing mucus volume and thickness.

**Stopping Infectious Pathogens**

N-acetyl-L-cysteine has been shown to reduce the number of harmful pathogens, including bacteria and viruses.

In the case of harmful bacteria, N-acetyl-L-cysteine makes it hard for them to gain a foothold and cause infection.

In vitro experiments show that N-acetyl-L-cysteine prevents bacteria from adhering to cells lining the airways.

One of the ways it accomplishes this is by disrupting biofilms, slimy coverings that many disease-causing bacteria form around themselves. These films prevent immune cells from recognizing and gaining access to the bacteria. They also make it difficult for antibiotics, antibodies, and other helpful compounds to get to the bacteria.

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**WHAT YOU NEED TO KNOW**

**N-Acetyl-L-Cysteine Supports the Lungs and Airways**

- **N-acetyl-L-cysteine** is a precursor to glutathione.
- It reduces and thins excess mucus production in the airways, which can be a major contributor to lung problems in infection and other conditions.
- N-acetyl-L-cysteine also reduces harmful inflammation and could help prevent colonization by viruses and bacteria in the lungs.
- Through all these mechanisms, N-acetyl-L-cysteine supports healthy respiratory tract function and may prevent or treat bronchitis, chronic obstructive pulmonary disease, acute respiratory distress syndrome, and respiratory tract infections.
- Typical daily doses of N-acetyl-L-cysteine range from 600 mg to 1,800 mg in divided doses.
N-acetyl-L-cysteine blocks the formation of biofilms and destroys existing ones, impeding the ability of bacteria to survive in the airways.\textsuperscript{2,3}

The protection from pathogens also extends to viruses.

One cell study evaluated respiratory syncytial virus. Normally, this virus invades the cells lining the airways, growing rapidly and causing damage to the structure of the airways.

But treatment with N-acetyl-L-cysteine blocks the reproduction of the virus while restoring the normal structure and function of the cells lining the airways.\textsuperscript{1}

Reducing Harmful Inflammation

By preventing free-radical damage, reducing pathogen colonization, and other mechanisms, N-acetyl-L-cysteine decreases harmful inflammation, which contributes to the symptoms of most respiratory disorders.

Preclinical studies show that N-acetyl-L-cysteine reduces the production of pro-inflammatory compounds and decreases the production of compounds that initiate fibrosis in the lung tissue, scarring that makes it difficult for the lungs to work properly.\textsuperscript{25-27}

Respiratory Tract Disorders

N-acetyl-L-cysteine has shown success in treating a number of different respiratory conditions.

**Chronic bronchitis** is longstanding inflammation in the airways of the lungs caused by irritation and tissue damage. It’s common in smokers but can also be caused by secondhand smoke, air pollution, and other inhaled irritants.

Several human studies have shown that oral intake of N-acetyl-L-cysteine reduces exacerbations (worsening or flare-ups) of chronic bronchitis and significantly improves symptoms.\textsuperscript{11,12}

**Chronic obstructive pulmonary disease (COPD)** refers to disorders of the lungs that restrict airflow in the lungs, making it hard to breathe. It includes chronic bronchitis, emphysema, and severe asthma.\textsuperscript{28,29}

Oxidative stress, inflammation, and excessive secretion of airway-clogging mucus play major roles in these conditions. Knowing that N-acetyl-L-cysteine helps prevent or treat all three of these problems, scientists have tested it to treat COPD.

In COPD patients, N-acetyl-L-cysteine use has been associated with clinical improvements. These include lower rates and decreased severity of exacerbations, and fewer days spent in the hospital for COPD exacerbations.\textsuperscript{4,13-18}
Acute respiratory distress syndrome (ARDS) is a form of severe lung inflammation that causes fluid to leak into the lungs, preventing oxygen from getting into the body.

It occurs in critical illness, particularly in patients suffering from pneumonia or other serious lung infections. It often requires mechanical ventilation and typically results in a high mortality rate.

Animal studies show that N-acetyl-L-cysteine protects the lungs from injury and leads to significant improvements. In clinical studies, patients with acute respiratory distress syndrome who were given N-acetyl-L-cysteine had shorter intensive-care-unit stays, and clinical improvements.

Summary
N-acetyl-L-cysteine (NAC) is a precursor to the antioxidant glutathione. It helps prevent harmful oxidative damage and reduces inflammation.

In the lungs and airways of the respiratory tract, it reduces and thins excess mucus secretion and could help prevent colonization by harmful bacteria and viruses.

Through these mechanisms and more, N-acetyl-L-cysteine supports healthy respiratory function and provides protection against lung diseases, including acute respiratory distress syndrome, infections, and chronic obstructive pulmonary diseases like bronchitis and emphysema.

Most individuals gain benefits from using 600 mg to 1,800 mg/day of N-acetyl-L-cysteine in divided dosages.

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

References


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N-ACETYL-L-CYSTEINE
Supports Healthy
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N-Acetyl-L-Cysteine (NAC) supports healthy levels of glutathione, a molecule utilized by all cells for protection against free-radical damage and attacks from pathogens.

NAC is a powerful antioxidant that helps clear airways, and benefits bronchial, respiratory, liver, and immune health.

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Caution: Those who supplement with NAC should drink 6 to 8 glasses of water daily in order to prevent cysteine renal stones. Cysteine renal stones are rare but do occur.

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Enhancing the Health Benefits of FISH OIL

BY MICHAEL DOWNEY
The benefits of the Mediterranean diet are well established. They include reduced cardiovascular and neurological risks along with lower overall mortality.\textsuperscript{1-7}

Components of the Mediterranean diet are comprised of fish, olive oil, nuts and seeds, vegetables and fruits, and whole grains.

Science today enables people to receive many Mediterranean diet components using concentrated:

- Fish oil rich in EPA/DHA
- Olive fruit and leaf extract
- Sesame seed lignan extract

To conveniently deliver these nutrients, researchers have combined fish oil, olive polyphenols, and sesame lignans to enhance overall health benefits.
The omega-3 fatty acids found in fish oil have a wide range of benefits for human health and longevity. Populations that consume large amounts of oily fish have reduced incidence of cardiovascular disorders, which include heart attacks, hypertension, strokes, atrial fibrillation, and heart failure.8-11

A meta-analysis found that the highest consumption of the omega-3s EPA and DHA is associated with a 14% reduction in the risk of dying from any cause, compared to the lowest omega-3 consumption.12

In the analysis, each additional 200 mg of fish oil consumed per day led to a 7% reduction in the overall risk of death.12

Fish oil works in many different ways to achieve these benefits.

It helps lower levels of triglycerides, fats linked to risk of heart disease. It reduces the buildup of plaque on artery walls that restricts blood flow, and improves function of the endothelial cells that line blood vessels.8,9

Fish oil also combats chronic inflammation, which plays a key role in age-related disease.13,14 That helps prevent:15-23

- Metabolic disorders, such as obesity and diabetes,
- Cancer,
- Neurological disorders, such as depression and Alzheimer’s,
- Autoimmune diseases,
- Chronic kidney disease, and
- Non-alcoholic fatty liver disease (NAFLD).

Olive Extract

Olive oil has long been considered a crucial contributor to the Mediterranean diet’s benefits.24

Research shows that people who consume the most olive oil have a lower risk of dying from cardiovascular events, strokes, or any cause at all, compared to those who consume the least.25

Consuming olive oil daily may also protect against conditions ranging from Alzheimer’s and osteoporosis to skin aging and cancer.26-29

Polyphenols are beneficial components present in olive oil that include oleuropein, tyrosol, and hydroxytyrosol.30-32

Hydroxytyrosol is one of the most common polyphenols present in extra virgin olive oil.31 In people over age 65, those who ingest the highest amount of hydroxytyrosol have been shown to live, on average, 9.5 years longer.33

Extracts of the olive leaf, concentrated and standardized to provide maximum polyphenol content, have been shown to protect cultured heart-muscle cells from destruction caused by oxidative damage.34 In a study in aged rats, olive polyphenols decreased stress-induced tissue damage and boosted intracellular resistance systems.35

In a rat model of metabolic syndrome, olive extracts improved or normalized accumulation of fat in the abdomen and liver, excessive collagen deposits in the heart and liver, cardiac stiffness, poor glucose tolerance, and abnormal lipid profiles.36
Summary

People who follow a Mediterranean diet, typically rich in fish and olive oil, have lower risk of cardiovascular and neurological diseases, cancer, bone loss, and overall mortality.

Research indicates that fish oil rich in omega-3 fatty acids offers anti-inflammatory and disease-prevention benefits.

Based on the impressive findings about the Mediterranean diet, combining fish oil concentrate with olive extract and sesame lignans may enhance overall health benefits.

Unique Power of Sesame Seeds

Sesame seeds have long been a component of the Mediterranean diet, whether added to dishes or ground into tahini or hummus.

They contain high concentrations of polyphenols called lignans. They may reduce blood lipid levels, fight inflammation and cancer, neutralize free radicals, and enhance vitamin E bioavailability (absorbability).

Metabolism of sesame lignans by intestinal microflora creates other compounds, enterolactone and enterodiol, both of which may have protective effects against hormone-related diseases such as breast cancer.

Sesame lignans may help enhance the effects of omega-3s in the body, making them a complement to add to fish meals and fish oil supplements.

WHAT YOU NEED TO KNOW

Combining Fish Oil, Olive Polyphenols, and Sesame Lignans

- The Mediterranean diet is high in fish, olive oil, seeds and nuts, and other wholesome plant-derived foods.
- People with greater adherence to this dietary pattern have reduced rates of cardiovascular and neurological diseases, cancer, and overall mortality.
- Science has allowed us to combine key components of the Mediterranean diet into a fish oil concentrate with olive extract and sesame lignans to enhance its health benefits.

People who follow a Mediterranean diet, typically rich in fish and olive oil, have lower risk of cardiovascular and neurological disorders, cancer, bone loss, and overall mortality.

Research indicates that fish oil rich in omega-3 fatty acids offers anti-inflammatory and disease-prevention benefits.

Based on the impressive findings about the Mediterranean diet, combining fish oil concentrate with olive extract and sesame lignans may enhance overall health benefits.

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.
Omega-3 Supplementation Reduces Cardiovascular Disease Death

The Mayo Clinic Proceedings recently published a meta-analysis showing that omega-3 supplementation is associated with significant reductions in the risk for cardiovascular disease death.42 The study looked at 40 clinical trials and concluded that supplementation with EPA and DHA reduced risk of coronary heart disease, including heart attack.

Specifically, the study found that EPA+DHA supplementation is associated with a reduced risk of:

- Fatal myocardial infarction (35%)
- Myocardial infarction (13%)
- Coronary heart disease events (10%)
- Coronary heart disease mortality (9%)

The cardiovascular protection was greater with increases in omega-3 dosage.

Increasing intake of EPA and DHA by 1,000 mg per day was associated with a reduction of 5.8% in the risk of cardiovascular disease events.

Robust evidence suggests benefits from daily supplementation with EPA+DHA. Today's fish oil products deliver a higher content of EPA/DHA per serving. Aging adults should consider taking at least 1,400 mg of EPA and 1,000 mg of DHA daily with meals that contain some fat to facilitate absorption.

References


41. Liu Z, Saarinen NM, Thompson LU. Sesamin is one of the major precursors of mammalian lignans in sesame seed (Sesamum indicum) as observed in vitro and in rats. *J Nutr.* 2006 Apr;136(4):906-12.

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Omega-3s are widely used to protect heart health.

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01985 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 enteric coated softgels
01984 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 enteric coated softgels
01986 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 240 softgels
01812 Provinal® Purified Omega-7
01640 Vegetarian DHA

FOOD
02008 California Estate Extra Virgin Olive Oil
02170 Rainforest Blend Decaf Ground Coffee
02169 Rainforest Blend Ground Coffee
02171 Rainforest Blend Whole Bean Coffee
00438 Stevia™ Organic Liquid Sweetner
00432 Stevia™ Sweetener

GLUCOSE MANAGEMENT
01503 CinSulin® with InSea 2® and Crominex® 3+
01620 CoffeeGenic® Green Coffee Extract
02122 Glycemic Guard™
00925 Mega Benfotiamine
01803 Tri Sugar Shield®

HEART HEALTH
01066 Aspirin (Enteric Coated)
01842 BioActive Folate & Vitamin B12 Caps
01700 Cardio Peak™ with Standardized Hawthorn and Arjuna
02121 Homocysteine Resist
02018 Optimized Carnitine
01949 Super-Absorbable CoQ10 Ubiquinone with d-Limonene • 50 mg, 60 softgels
01951 Super-Absorbable CoQ10 Ubiquinone with d-Limonene • 100 mg, 60 softgels
01929 Super Ubiquinol CoQ10
01427 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 30 softgels
01425 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 100 softgels
01437 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 30 softgels
01426 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 60 softgels
01431 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 200 mg, 30 softgels
01733 Super Ubiquinol CoQ10 with PQQ
01859 TMG Liquid Capsules
00349 TMG Powder

HORMONE BALANCE
00454 DHEA (Dehydroepiandrosterone) 15 mg, 100 capsules
00335 DHEA (Dehydroepiandrosterone) 25 mg, 100 capsules
00882 DHEA (Dehydroepiandrosterone) 50 mg, 60 capsules
00607 DHEA (Dehydroepiandrosterone) 25 mg, 100 vegetarian dissolve in mouth tablets
01689 DHEA (Dehydroepiandrosterone) 100 mg, 60 veg capsules
02368 Optimized Broccoli and Cruciferous Blend
00302 Pregnenolone • 50 mg, 100 capsules
00700 Pregnenolone • 100 mg, 100 capsules
01468 Triple Action Cruciferous Vegetable Extract
01469 Triple Action Cruciferous Vegetable Extract with Resveratrol

IMMUNE SUPPORT
02411 5 Day Elderberry Immune
00681 AHCC®
02302 Bio-Quercetin
02410 Black Elderberry + Vitamin C
01961 Enhanced Zinc Lozenges
01704 Immune Modulator with Tinofend®
00955 Immune Protect with PARACTIN®
02005 Immune Senescence Protection Formula™
29727 Kinoko® Gold AHCC
24404 Kinoko® Platinum AHCC
00316 Kyolic® Garlic Formula 102
00789 Kyolic® Reserve
01681 Lactoferrin (Apolactoferrin) Caps
01903 NK Cell Activator™
01394 Optimized Garlic
01309 Optimized Quercetin
01811 Peony Immune
00525 ProBoost Thymic Protein A
01708 Reishi Extract Mushroom Complex
01906 Standardized Cistanche
13685 Ten Mushroom Formula®
01097 Ultra Soy Extract
01561 Zinc Lozenges

INFLAMMATION MANAGEMENT
01639 5-LOX Inhibitor with AprèsFlex®
02324 Advanced Curcumin Elite™ Turmeric Extract, Ginger & Turmerones
01709 Black Cumin Seed Oil
02310 Black Cumin Seed Oil and Curcumin Elite™ Turmeric Extract
00202 Boswellia
02467 Curcumin Elite™ Turmeric Extract • 30 veg capsules
02407 Curcumin Elite™ Turmeric Extract • 60 veg capsules
01804 Cytokine Suppress® with EGCG
02223 Pro-Resolving Mediators
00318 Serraflazyme
01203 Specially-Coated Bromelain
00407 Super Bio-Curcumin® Turmeric Extract
01254 Zyflamend™ Whole Body

JOINT SUPPORT
02404 Arthro-Immune Joint Support
02238 ArthroMax® Advanced NT2 Collagen™ & AprèsFlex®
01617 ArthroMax® with Theaflavins & AprèsFlex®
02138 ArthroMax® Elite
00965 Fast-Acting Joint Formula
00522 Glucosamine/Chondroitin Capsules
01600 Krill Healthy Joint Formula
01050 Krill Oil
00451 MSM (Methylsulfonylmethane)
02231 NT2 Collagen™

KIDNEY & BLADDER SUPPORT
00862 Cran-Max® Cranberry Whole Fruit Concentrate
01424 Optimized Cran-Max® with Ellirose™
01921 Uric Acid Control
01209 Water-Soluble Pumpkin Seed Extract

LIVER HEALTH & DETOXIFICATION
01922 Advanced Milk Thistle • 60 softgels
01925 Advanced Milk Thistle • 120 softgels
02240 Anti-Alcohol Complex
01651 Calcium D-Glucarate
00550 Chlorella
01571 Chlorophyllin
01522 Milk Thistle • 60 veg capsules
02402 FLORASSIST™ Liver Restore™
01541 Glutathione, Cysteine & C
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PRODUCTS

80137  All-Purpose Soothing Relief Cream
80139  Amber Self MicroDermAbrasion
80118  Anti-Aging Mask
80176  Collagen Boosting Peptide Cream
80156  Collagen Boosting Peptide Serum
02408  Collagen Peptides for Skin & Joints
80169  Cucumber Hydra Peptide Eye Cream
80141  DNA Support Cream
80163  Eye Lift Cream
80123  Face Rejuvenating Anti-Oxidant Cream
80109  Hyaluronic Facial Moisturizer
80110  Hyaluronic Oil-Free Facial Moisturizer
80138  Hydrating Anti-Oxidant Facial Mist
00661  Hydroderm
80103  Lifting & Tightening Complex
80168  Melatonin Advanced Peptide Cream
80114  Mild Facial Cleanser
80172  Multi Stem Cell Hydration Cream
80159  Multi Stem Cell Skin Tightening Complex
80164  Skin Tone Equalizer
80143  Stem Cell Cream with Alpine Rose
80166  Skin Firming Complex
80130  Skin Stem Cell Serum
80129  Skin Stem Cell Serum
80113  Under Eye Refining Serum
80104  Under Eye Rescue Cream
80171  Vitamin C Lip Rejuvenator
80136  Vitamin D Lotion
80102  Vitamin K Cream

SLEEP
01512  Bioactive Milk Peptides
02300  Circadian Sleep
01551  Enhanced Sleep with Melatonin
01511  Enhanced Sleep without Melatonin
02234  Fast-Acting Liquid Melatonin
01669  Glycine
02308  Herbal Sleep PM
01722  L-Tryptophan
01668  Melatonin • 300 mcg, 100 veg capsules
01083  Melatonin • 500 mcg, 200 veg capsules
00329  Melatonin • 1 mg, 60 capsules
00330  Melatonin • 3 mg, 60 veg capsules
00331  Melatonin • 5 mg, 60 veg capsules
02201  Melatonin IR/XR
01787  Melatonin 6 Hour Timed Release 300 mcg, 100 veg tablets
01788  Melatonin 6 Hour Timed Release 750 mcg, 60 veg tablets
01786  Melatonin 6 Hour Timed Release 3 mg, 60 veg tablets

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

WEIGHT MANAGEMENT & BODY COMPOSITION
00658  7-Keto® DHEA Metabolite • 25 mg, 100 capsules
02479  7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules
01509  Advanced Anti-Adipocyte Formula
01807  Advanced Appetite Suppress
02207  AMPK Metabolic Activator
02478  DHEA Complete
01738  Garcinia HCA
01292  Integra-Lean®
01441  Optimized Saffron with Satiereal®
00818  Super CLA Blend with Sesame Lignans
02204  Vitamins D and K with Sea-Iodine™

WOMEN’S HEALTH
01942  Breast Health Formula
01626  Enhanced Sex for Women 50+
01894  Estrogen for Women
01064  Femmenessence MacaPause®
02043  Optimized Saffron with Satiereal®
00818  Super CLA Blend with Sesame Lignans
01902  Waist-Line Control™
02151  Wellness Code® Appetite Control
Humans don’t manufacture **vitamin C** internally, so it must be obtained through dietary sources or supplements.

**Vitamin C** is water soluble and needs to be constantly replenished.*

A highly **absorbable** form of **quercetin** complements vitamin C’s activity in the body.

Each tablet provides 1,000 mg of **vitamin C** and 15 mg of **Bio-Quercetin Phytosome**.

**SUPER SALE PRICE**

**Item #02227** • 250 vegetarian tablets
1 bottle $20.25 • 4 bottles $18 each

For full product description and to order **Vitamin C and Bio-Quercetin Phytosome**, call 1-800-544-4440 or visit www.LifeExtension.com


These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Clinically validated ingredients help maintain cartilage and inhibit inflammatory factors to support joint health.

**J JUST TWO CAPSULES A DAY PROVIDE:**

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

NT2 Collagen™ is manufactured by Bioibérica. AprèsFlex® is a registered trademark of Laila Nutraceuticals exclusively licensed to PL Thomas - Laila NUTRA LLC. U.S. Patent No. 8,551,496 and other patents pending. FruiteX-B® and OsteoBoron® are registered trademarks of VDF FutureCeuticals, Inc. U.S. Patent No. 5,962,049.

² 3-O-acetyl-4-keto-B-boswellic acid.

**SUPER SALE PRICE**

Item #02238 • 60 capsules

1 bottle $22.95

4 bottles $19.80 each

For full product description and to order **ArthroMax® Advanced with NT2 Collagen™ & AprèsFlex®**, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
**PQQ** (pyrroloquinoline quinone) activates genes involved in the production of cellular energy.¹⁻⁵

Studies show **PQQ** supports heart health and cognitive function, complementing **CoQ10**.⁶⁻⁷

In fact, just **20 mg** per day of **PQQ** plus **CoQ10** promotes memory and attention in aging individuals.⁸

This formulation contains **20 mg** of **PQQ** per capsule, which is the recommended daily dose.

For full product description and to order **PQQ** or any other **PQQ-containing formulas**, call 1-800-544-4440 or visit www.LifeExtension.com

Also available are **10 mg PQQ caps** (Item #01500) and **100 mg Super Ubiquinol CoQ10 with PQQ** (Item #01733).

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**References**


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

Want to feel your best? Digestive health is key.

The 7-strain blend in FLORASSIST® GI with Phage Technology helps maintain healthy digestion, microbiome balance, and nutrient absorption.

Plus, the phage blend targets bad bacteria, leaving you with more beneficial probiotics.

Trust your gut: FLORASSIST® GI with Phage Technology.

SUPER SALE PRICE
Item #02125
30 liquid vegetarian capsules

1 bottle $22.28
4 bottles $20.25 each

For full product description and to order FLORASSIST® GI with Phage Technology, call 1-800-544-4440 or visit www.LifeExtension.com

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

PROTECT RESPIRATORY FUNCTION
NAC (N-acetyl-L-cysteine) helps prevent viruses and bacteria from adhering to the lining of the lungs, while reducing excess airway mucus.

FISETIN: A LONGEVITY SENOLYTIC
In an animal study, fisetin increased lifespan. It also functions as a powerful senolytic. A new fisetin formula provides 25 times greater bioavailability.

HIGH-DOSE VITAMIN K2 BUILDS NEW BONE
Japanese physicians prescribe high-dose vitamin K2 to treat osteoporosis. Now available without a prescription, 45 mg of vitamin K2 increases bone density and reduces fracture risk.

THWART POST-MEAL BLOATING
Up to 30% of people complain about after-meal bloating. Researchers have identified plant compounds that relieve gastrointestinal distress.

"I WAS NOT SURPRISED TO HAVE OSTEOPENIA"
Aging is almost always accompanied by bone loss. Bill Faloon reports on his diagnosis.

ENHANCING THE BENEFITS OF FISH OIL
Scientists combined key components of the healthy Mediterranean diet into a fish oil concentrate with olive extract and sesame lignans.

Annual SUPER SALE begins November 9, 2020