

Vitamin K₂

A complete primer.

Why it's important.
How it works.
How it can help you.

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Thanks again, and please enjoy the read!

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Vitamin K2

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How it works.

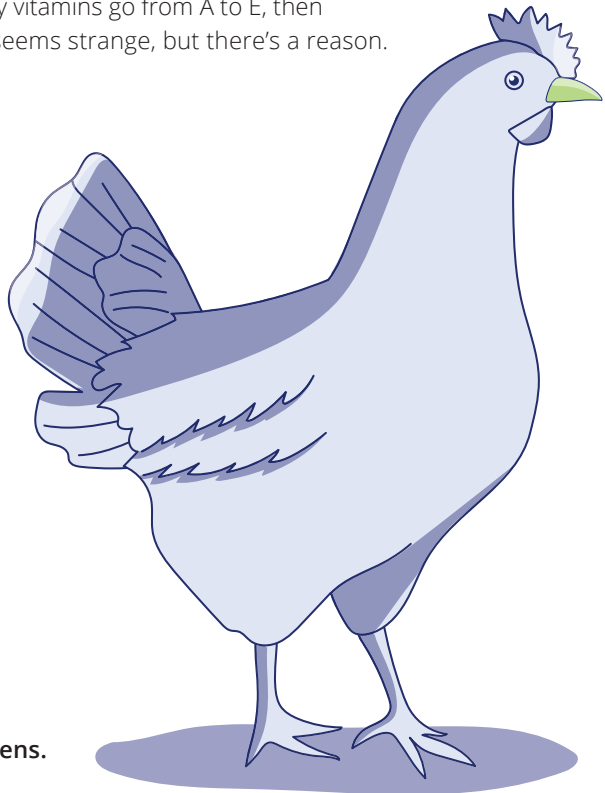
How it can help you.

What's inside

Vitamin what?	3	Can't get enough of a good thing	31
A brief history of the little-known, misunderstood vitamin	5	Am I getting enough Vitamin K2?	36
Vitamin K2 is not K1!	11	What form of vitamin K2 should I take?	42
The biochemical secret to vitamin K2's power	14	CanPrev Vitamin K2	49
Vitamin K2's role in the body	26	About CanPrev	55

Vitamin what?

Ever wonder why vitamins go from A to E, then straight to K? It seems strange, but there's a reason.



It involves **chickens**.

In 1929, a Danish nutritional scientist named Dr. Henrik Dam was studying the effects of cholesterol. During this study, he noticed that chickens who were put on a fat-free diet became ill and suffered from uncontrolled bleeding and bruising.

When the bleeding didn't stop after restoring cholesterol to their diets, Dr. Dam realized that there must be another fat-soluble nutrient in their old diet that controlled blood clotting. With a bit of effort, he identified this nutrient and named it vitamin K, for koagulation (Danish for coagulation!)

Our understanding of vitamin K has flourished in the 90 years since Dr. Dam's discovery. Today, we know that vitamin K isn't just one vitamin, but a family of fat-soluble vitamins that share a similar molecular structure. And mounting clinical evidence over the past two decades has shown its role in human health goes well beyond blood clotting. Vitamin K (and in particular, vitamin K2) plays an essential role in cardiovascular and bone health. New research shows promising links to other health benefits like adolescent growth, blood sugar support, pregnancy, kidney health and even aging skin.

Despite all these advances in research, it is still one of the most misunderstood nutrients in medicine today.

We've put together this primer to clear up some common misconceptions of vitamin K. And we hope that by reading this, you'll better understand what vitamin K is, appreciate what it can do for your body, know which forms to choose, and how to best use it for your continued good health.



Timeline of Vitamin K

1600s



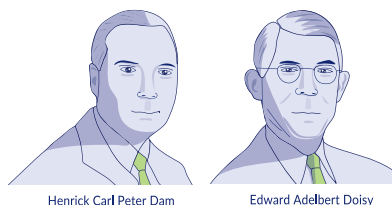
Samurai warriors in feudal Japan consume a fermented soybean dish called natto, a potent source of vitamin K2.

A brief history of the little-known, misunderstood vitamin

Why does confusion about vitamin K linger to this day?

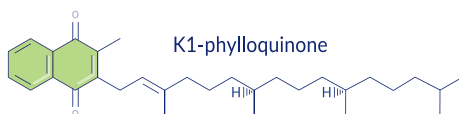
Dam & Doisy's Mistake

Research on vitamin K persisted in the decade following Henrik Dam's initial discovery in 1935. In the late 1930s, an American researcher named Edward Doisy succeeded in isolating vitamin K, isolating its molecular structure. This form later became known as vitamin K1.



Henrick Carl Peter Dam

Edward Adelbert Doisy



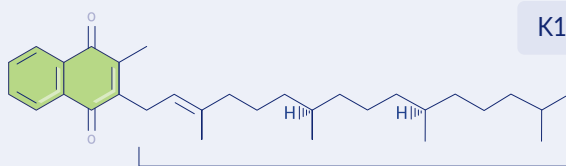
In 1943, Dam and Doisy shared a Nobel Prize in medicine for their discovery of this "coagulation" vitamin. Unfortunately, this recognition solidified many of the misunderstandings we see today.

You see, Dam, Doisy and other researchers at the time had already identified and characterized the structure of another micronutrient, vitamin K2. But it didn't occur to them to treat K1 and K2 as separate micronutrients, with different benefits and unique properties. Instead, K1 and K2 were considered to be simply structural variants of the same vitamin, with the same biological role.

1930s



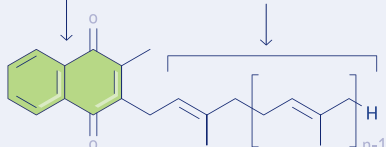
The vitamin K family is discovered. Danish scientist Dr. Henrik Dam describes a fat-soluble factor that reduces bleeding in chicks fed an extremely low-fat diet. He names this factor vitamin K, for koagulation. A few years later, American biochemist Edward Doisy determines the chemical structure of vitamin K and succeeds in synthesizing it.



K1-phyloquinone

Naphtaquinone ring

Side chain



K2-menaquinone

Looking at K1 and K2 side by side, you can imagine why Dam and Doisy thought they were variations of the same vitamin. All K vitamins have a naphthoquinone ring and a side chain of hydrogen and carbon atoms (called isoprenoids). Different forms of vitamin K have isoprenoid side chains of different lengths and saturation. We'll see later why these structural variations matter.

With the Nobel Prize, the fates of K1 and K2 became irrevocably intertwined for the next fifty years. All variations of vitamin K were only known for their role in blood clotting. A further corollary was established: all vitamin K deficiencies were rare and obvious, since it was assumed that a deficiency in vitamin K would result in some kind of bleeding disorder.

So final were these conclusions that little effort was spent to expand the body of vitamin K knowledge for the next thirty years. A big loss for vitamin K2, whose far greater role in the body was left undiscovered. Even worse, no one was looking for vitamin K2 deficiencies, which, as we now know, is quite widespread.

1943



Dam and Doisy share the 1943 Nobel Prize in Medicine for their pioneering work on vitamin K1.

1950s



Weston Price discovers 'Activator X' (K2) as a missing ingredient for tooth and bone health.



The Adventures of Dr. Weston Price and the Secret of **Activator X**

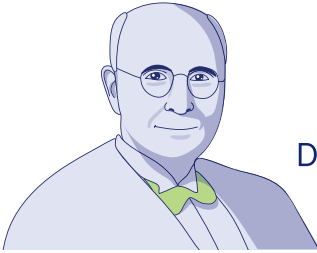


1960s

Vitamin K2 as MK-4
is approved as a
drug in Japan.

1970s

Dr. Cees Vermeer starts
researching the role of
vitamin K as a coenzyme and
its role in activating osteocalcin.



Dr. Weston Price

At the same time Dam and Doisy were conducting their research, mild-mannered Dr. Weston Price, a Canadian with a small dental practice in Ohio, wondered why so many of his patients had terrible teeth. He hypothesized that there was something about the rapidly modernizing diet that was linked to declining dental health. Dr. Price sought out pre-industrial populations scattered across the globe in an effort to study this relationship between tooth decay and nutrition.

In a series of perilous expeditions, he made his way to remote villages in the mountainous pockets of Switzerland, settlements along the rugged coasts of the Outer Hebrides, and the archipelagos of the South Pacific. He travelled with the nomadic Masai of Tanzania and the Nuer

of the South Sudan, New Zealand Maori, the Inuit of Alaska and the tribes of the Peruvian Amazon and Andes. He observed that populations that maintained their traditional diet did not suffer from the tooth decay or malocclusion that was rampant back home. Instead, he found square jaws with neat, straight rows of teeth. When the same families were introduced to common processed foods, they would develop cavities and dental decay.

Armed with a camera, he would take photos of siblings - where the older child was raised on a traditional indigenous diet and the younger was living on imported foods. The first child would have well formed dental arches, whereas the second would have many misaligned teeth.

1990s

Vitamin K2 is largely overlooked for a number of years before being rediscovered. Researchers in Japan begin to study the transfer of vitamin K2 between mothers and newborns.





Price took over 15000 photographs comparing teeth before and after a change in traditional diet

It was a predictable pattern linking diet with dental health. In addition to that, Price noticed several other symptoms of declining health, including slow healing bone fractures.

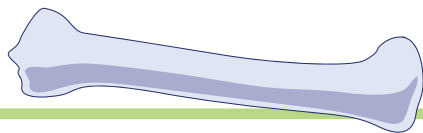
His fieldwork throughout the 1920s and 1930s yielded over 15,000 similar stark photographs. When he returned, he detailed his ethnographic and nutritional studies in a book called *Nutrition and Physical Degeneration*. Without the benefit of our understanding of modern nutrition, Price hypothesized that these declines in dental health were not the result of some toxin in American diet, but the “absence of some essential factors”. He tested and analyzed thousands of samples of traditional foods for their nutritional content and compared

them to common foods of the time. What he found was that many of the traditional foods, like fish eggs and the butterfat of grass-fed cows, were rich in fat-soluble nutrients.

He deduced that there was some activator or catalyst in the fat-rich diet that allowed the body to make use of other macronutrients like minerals. One activator had a significant effect on the health of bones and teeth, but since he could not identify or chemically isolate it, he labelled it as Activator X.

For years, physicians and nutritionists debated what this mystery Activator X could be. Some thought it might be a kind of essential fatty acid like EPA. Sixty years after Activator X was first mentioned, researchers now believe Activator X to be vitamin K2.

2000s



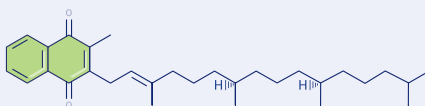
Studies investigate the relationship between K2, bone health and K2 biomarkers. During this time, researchers in Japan publish studies investigating the link between K2 and bone health. The impact of natto intake on bone stiffness and hip fractures is investigated.

Vitamin K2 MK-4 and MK-7

Vitamin K2 itself is not a single nutrient, but is itself a collection of molecules called menaquinones. These menaquinones share the same naphthoquinone ring as vitamin K1. However, while vitamin K1 has a monounsaturated side chain, menaquinones have unsaturated isoprenoid side chains of varying lengths.

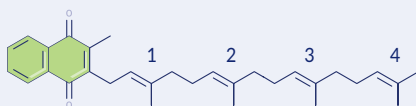
A menaquinone with four isoprenoid units is called MK-4, five units MK-5 and so on up to MK-14. The two most common menaquinones identified for human health are MK-4 and MK-7.

K1-phyllloquinone

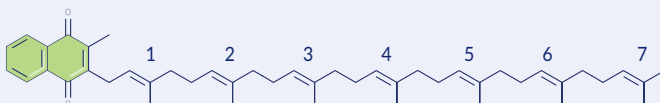


Menaquinones have side chains of different lengths. MK-4 has a length of 4 isoprenoid units. MK-7 has a length of 7 isoprenoid units.

MK-4



MK-7



MK-4 and MK-7 have some functional differences. The lengths of the side chains help determine the lifespan in the body. MK-4 has a much shorter half-life in the body than MK-7, passing through the body in a matter of hours. MK-7, with its much longer side chain, has a half-life of three days.

MK-7, with its longer half-life, is also capable of reaching more parts of the body than MK-4. While MK-4 is good at supporting the soft tissues in the body, MK-7 is able to reach and support the liver and bone.

2015

Studies in 2015 demonstrate reductions in arterial stiffness and the slowing of arterial calcification, thereby reducing cardiovascular risk.



Vitamin K2 is not K1!

It's probably a good idea before we go further to reiterate exactly why we focus on vitamin K2 in this book. Why K2 and not K1? And is this case of mistaken identity really such a big deal?

1. K2 has a different biological role than K1.

Vitamin K2 has a wide range of biological roles, and has better overall health benefits. Vitamin K1 is primarily used for blood coagulation. Vitamin K2 can also be used in blood coagulation, but has many more functions.

Vitamin K2 can prevent calcium from being deposited into soft tissues like the kidney, where it can cause kidney stones, or into arteries where it can increase the risk of heart disease.

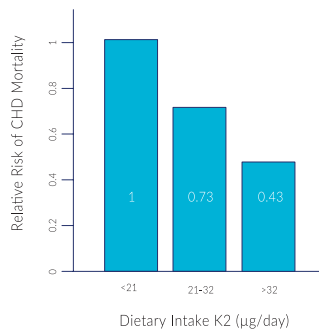
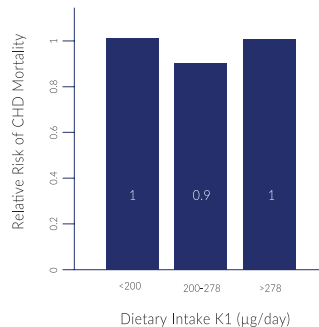
At the same time, vitamin K2 can help transport that same calcium into bones and teeth, improving bone density and strong teeth. Several observational and controlled studies have linked low levels of vitamin K2, especially of MK-7, with a higher incidence of fractures.

K1 does not have the same cardiovascular or bone benefits that K2 has. These functional differences between K1 and K2 have been demonstrated in recent studies.

For example, in the large scale Rotterdam Study, where 4807 subjects were observed over 7-10 years, those with the highest vitamin K2 intake compared to those with the lowest intake had a 57% reduction in the risk of dying

from cardiovascular disease. And their risk of having severe aortic calcification (narrowing of the heart's aortic valve) was slashed by 52%.

Despite study participants consuming ten times more dietary K1 than K2, K1 intake showed no influence on aortic calcification or the risk of cardiovascular disease.



The main body of research has focused on vitamin K2's influence on bone and heart health, but there are more studies underway to link K2 to

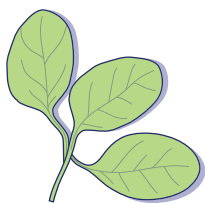
other roles like insulin metabolism, increasing testosterone in males and facilitating growth in adolescence.

Overall, the data suggests that K2, not K1, is the primary supporter of general health.

2. K1 and K2 come from different dietary sources. And we get a lot less K2 than K1.

Because of its role in photosynthesis, vitamin K1 is found mainly in the leaves of plants. Its scientific name, phyloquinone, reflects that, phyllo meaning leaves in Greek.

Present in leafy greens such as broccoli, kale and spinach, phyloquinone can be obtained through vegetables and vegetable oils. Vitamin K1 represents 90% of our total dietary intake in K vitamins.



In contrast, menaquinones, or vitamin K2, are mostly microbial in origin. Simpler microbial organisms like bacteria produce and use vitamin K2 for many different metabolic processes. We can expect to find K2 in sources with a lot of microbial activity, like animal products such as fermented cheese

and yogurt. (The first K2 isolates were in fact derived from putrefied fish meal.)

MK-4 form of vitamin K2 can be obtained from meat, dairy and eggs. MK-7 is mainly found in fermented foods like cheese, but it is particularly abundant in a Japanese dish of fermented soybeans called natto.

Unfortunately, the dietary intake of vitamin K2 has diminished over the past hundred years. Thanks to refrigeration and canning, we are eating less vitamin K2-rich fermented foods like cured fish and aged cheese. And thanks to industrial farming, animal sources aren't great sources of vitamin K2 either. Animals have the ability to convert K1 to K2 from the grasses they graze on, but grain-fed animals are not consuming enough K1.

3. Signs of deficiency are different.

Unlike vitamin K1, it is possible to have a vitamin K2 deficiency without signs of overt bleeding or bruising. As vitamin K2 is heavily involved in cardiovascular and bone health, which are considered silent diseases, the signs of vitamin K2

deficiency often remain undetected until it is too late. Waning bone density or plaque buildup in arteries (composed of calcium, fat, cholesterol, etc.) may take years before they are detected.

It's important to understand these differences because sometimes the differences aren't so clear cut. And the occasional similarities tend to confuse the issue about which forms you need.

For example, there are studies that show that all vitamin Ks can promote healthy bones. However, vitamin K1 and MK-4 vitamin K2 show effectiveness only at high doses compared to MK-7 vitamin K2.

There's also the argument that since animals break down and convert vitamin K1 into MK-4 vitamin K2, humans can too. Therefore, the kind of vitamin K we consume doesn't matter. There are two problems with this argument. First, we don't know enough about this conversion

process to gauge how good humans are at turning K1 into K2 compared to other animals.

Second, if we could efficiently convert between the different forms, it shouldn't matter which vitamin K to consume. Studies are showing otherwise. If there are no limitations, then research like the Rotterdam study would show that both K1 and K2 consumptions would have an effect on aortic calcification. However, only K2 demonstrated an effect.

So yes, vitamin K2 is quite different from K1. And it is something a lot of us could use more of.

Let's see why.

What if I don't see any symptoms? Silent deficiencies & triage theory.

Sometimes micronutrient deficiencies may not exhibit the usual array of signs and symptoms. Why does this happen?

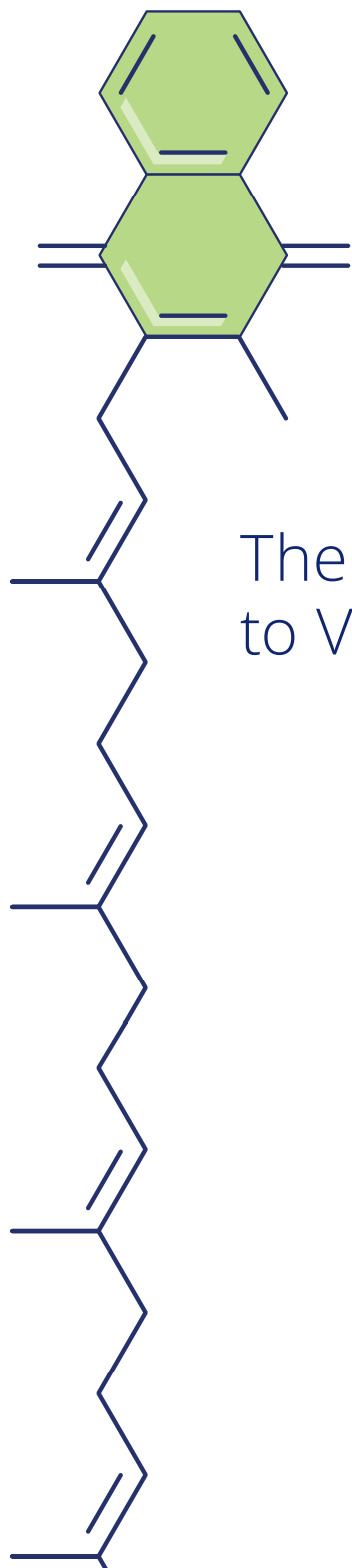
Dr. Bruce Ames is a professor emeritus of molecular biology at the University of California, Berkeley and a senior scientist at the Children's Hospital Oakland Research Institute. In his research on degenerative diseases, he noted that deficiencies in various micronutrients may lead to DNA damage and cellular aging. He theorized that this was the consequence of something called triage allocation.

Organisms (like humans) commonly live through episodes of micronutrient shortages. Triage allocation theory hypothesizes that during those

shortages, scarcer micronutrients are allocated towards urgent short-term survival at the expense of sustaining long-term health. For example, a shortage of iron will draw from stores in the liver before it draws critical iron stores in the heart.

In the case of vitamin K deficiencies, the body would allocate what little it has to support critical blood coagulation enzymes in the liver at the expense of bone building functions.

Triage theory: Rebalancing micro-nutrients for short-term survival at the expense of long-term health.



The biochemical secret
to Vitamin K2's power

Activator X's secret identity is vitamin K2? And it plays a key role in bone and teeth health?

The notion of vitamin K2's expanded role into bone health (and later cardiovascular health) seemed bizarre. How were these connected to vitamin K2's original role as a blood coagulation aid? And what about all of these other health benefits we are just discovering now?

To explain that, we need to understand a little bit about how vitamins work on a fundamental level.

Vitamins activate enzymes.

We are kept alive by trillions of chemical reactions that occur in the body. Carbohydrates are broken up and harvested for energy. New tissue is created. Cellular waste products are removed. New strands of DNA are made. This collection of chemical processes is called metabolism.

The speed that a reaction occurs will depend on factors like temperature, pressure, solubility and concentration of molecules. We use these factors every day. You might notice that sugar dissolves in hot water faster, or putting food in the refrigerator will slow the rate of decay. When you make a campfire, a hotter flame will use up wood faster.

Our metabolism needs to occur at a certain speed to stay alive. But we don't have the liberty of turning the

body into a raging furnace to speed up these reactions (not without damaging the body). That's where enzymes come in.

Enzymes are bits of protein that catalyze and regulate almost all metabolic reactions. As catalysts, they reduce the energy needed to spark a chemical reaction. They speed up the rates of reaction. Without enzymes, reactions that would normally take milliseconds might take hours or days.

Some enzymes require helpers called cofactors to ignite a reaction. Without a cofactor bound to its structure, an enzyme may float dormant and inactive, unable to catalyze any reactions. All vitamins serve as cofactors for enzyme proteins. When a vitamin is absent, the proteins that depend on it are left inactive.

How slow are reactions without enzymes?

How long would reactions take if they proceeded spontaneously without the presence of enzymes? Dr. Richard Wolfenden, an alumni professor of biochemistry & biophysics at the University of North Carolina, posed this question. In a 1995 study, Wolfenden reported that without enzymes, the process of synthesizing DNA and RNA would take 78 million years. A subsequent study in 2008 found that producing cellular hemoglobin in the absence of enzymes would be thirty times slower, with a half-life of 2.3 billion years. That's half the age of the Earth!



How do K vitamins activate enzymes?

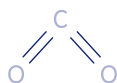
All vitamins activate protein enzymes a little differently. K vitamins activate proteins through a process called gamma-glutamyl carboxylation.

Sounds complicated? Don't worry - it's just a technical way of saying that vitamin K attaches carbon dioxide to a specific site on a vitamin K dependent protein. Let's break it down.

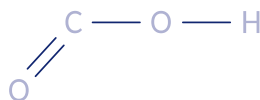
Carboxylation

We are familiar with CO₂ as carbon dioxide, the stuff we exhale. Inside the body, CO₂ is dissolved in our blood and tissues, making it an ion with a negative charge. We call this form a carboxyl group (COO⁻).

Carbon dioxide



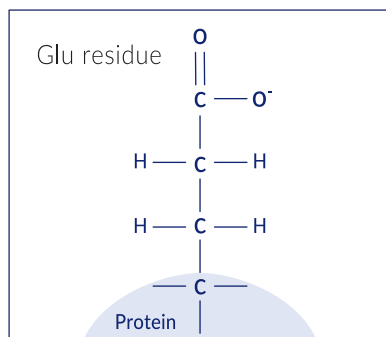
Carboxyl group



Carboxylation is the act of attaching a carboxyl group to another molecule. Decarboxylation is the process of removing a carboxyl group from a molecule.

Glutamic acid

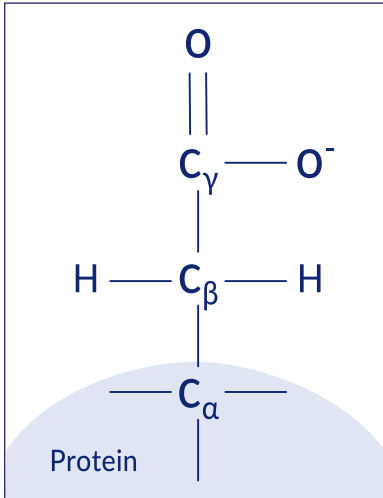
Proteins are made up of chains of amino acids. Glutamic acid is one such amino acid, made up of three carbon atoms and one carboxyl group. This is the part of the protein that vitamin K attaches a carboxyl group to.



When glutamic acid is part of a protein, it's also known as a glutamate or "Glu" residue.

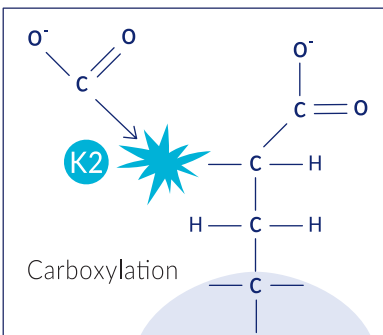
Gamma

Gamma just refers to which carbon atom in the glutamate residue we are attaching the carboxylic acid to. Sort of like a street address. In this case, gamma refers to the third carbon in the side chain.

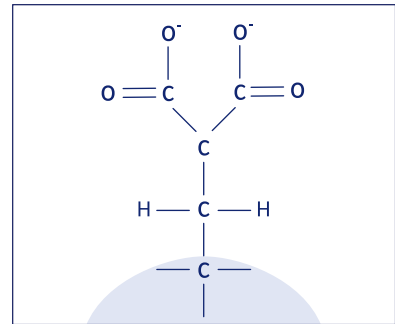


Gamma-glutamyl carboxylation

Let's put it all together. Vitamin K attaches a carboxyl group to the third carbon of a glutamate residue. This modified glutamate structure is called a gamma-carboxyglutamate or "Gla" residue.

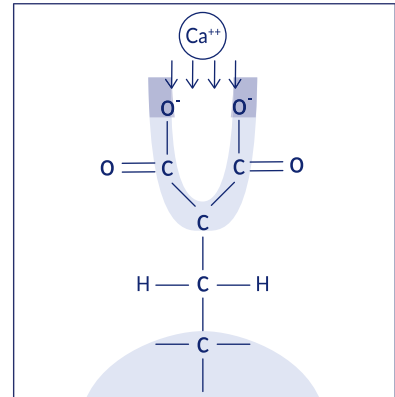


Once activated, this Gla residue has two carboxyl groups attached to the gamma carbon.



γ Carboxyglutamate (Gla)

This gives the residue two negative charges, which is ideal for binding (or attracting) calcium ions, which have two positive charges. This calcium manipulation, as we'll see later, is the key.



Gla sites attract calcium

When you hear biochemists talk about vitamin K dependent proteins, you may hear them refer to the protein as **gamma-carboxylated (gla/gc)** or **undercarboxylated (uc)**.

They're just indicating whether the enzyme is activated or not.

Vitamin K Dependent Proteins (VKDPs)

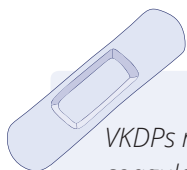
Vitamin K dependent proteins (VKDPs) are found throughout the body in different tissues. Scientists have now identified 17 different VKDPs that undergo the same carboxylation process but fulfill different functions. Some help with building up the bone matrix. Some prevent arteries from calcifying (and hardening). Others increase insulin sensitivity, renew tissue, control cell growth or sweep dead cells away. They are present in a wide variety of tissues, such as bone, kidney, placenta, pancreas, spleen, lung, and blood vessel walls.

We haven't even figured out what some VKDPs do yet, and we are still discovering new VKDPs.

VKDPs for blood coagulation

Seven VKDPs, known as clotting factors, regulate blood coagulation. They are made in the liver and released into the bloodstream, inactive until needed. When injury occurs, these clotting factors activate, transforming fibrinogen (also present in plasma) into fibrin. When fibrin is combined with blood platelets, it forms a clot.

While vitamin K2 is circulated to other tissues and organs in the body, vitamin K1 is found primarily inside the liver, which is why K1's role is so tightly bound to blood coagulation.



VKDPs responsible for blood coagulation: prothrombin (factor II), factors VII, IX, and X, and proteins C, S, and Z

Osteocalcin for bones, fractures, hormones and metabolism

Vitamin K2 is used in the activation of a protein called osteocalcin (OC). This VKDP, discovered in 1975, was the first hint of vitamin K2's greater role in the body.

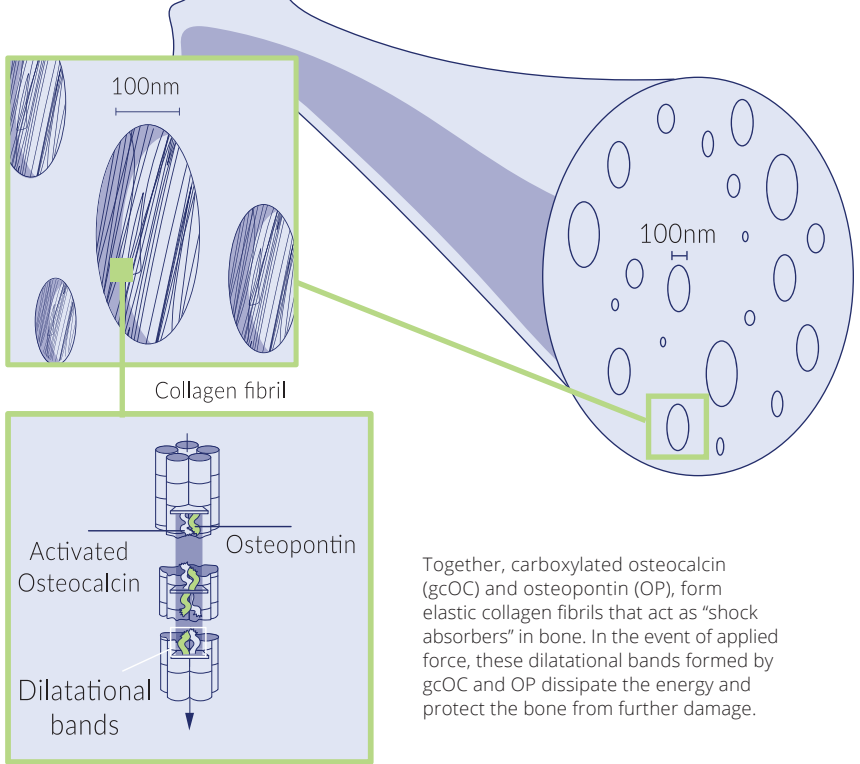


+ ucOC \longrightarrow gcOC

Osteocalcin is produced in bones and teeth where, when activated by vitamin K2, it helps to transport and integrate calcium into the bone matrix. Carboxylated osteocalcin binds to the calcified matrix of bone tissue. Although this was one of the first functions identified, osteocalcin's role in bone mineralization and architecture is still being investigated.

Fractures

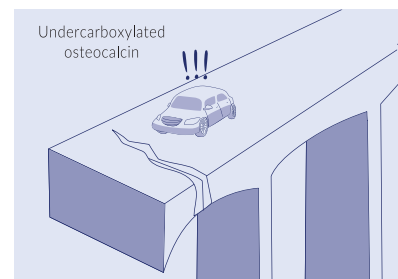
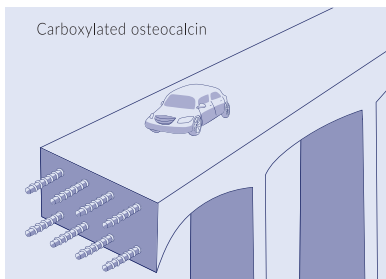
One recent line of investigation has suggested that osteocalcin, along with another protein called



Together, carboxylated osteocalcin (gcOC) and osteopontin (OP), form elastic collagen fibrils that act as “shock absorbers” in bone. In the event of applied force, these dilatational bands formed by gcOC and OP dissipate the energy and protect the bone from further damage.

osteopontin, helps to prevent crack growth in bone fractures. Carboxylated osteocalcin and osteopontin combine to form elastic collagen fibrils in bone. These fibril bands act as shock absorbers or springs, making bones a little more flexible.

When a bone is subjected to bending force, tiny 100nm voids appear in the bone matrix. The osteocalcin-osteopontin fibrils stretch to form dilatational bands in the voids, dissipating the energy and preventing greater damage. When the stress subsides, the bands can close and the nanoscale holes can be repaired.



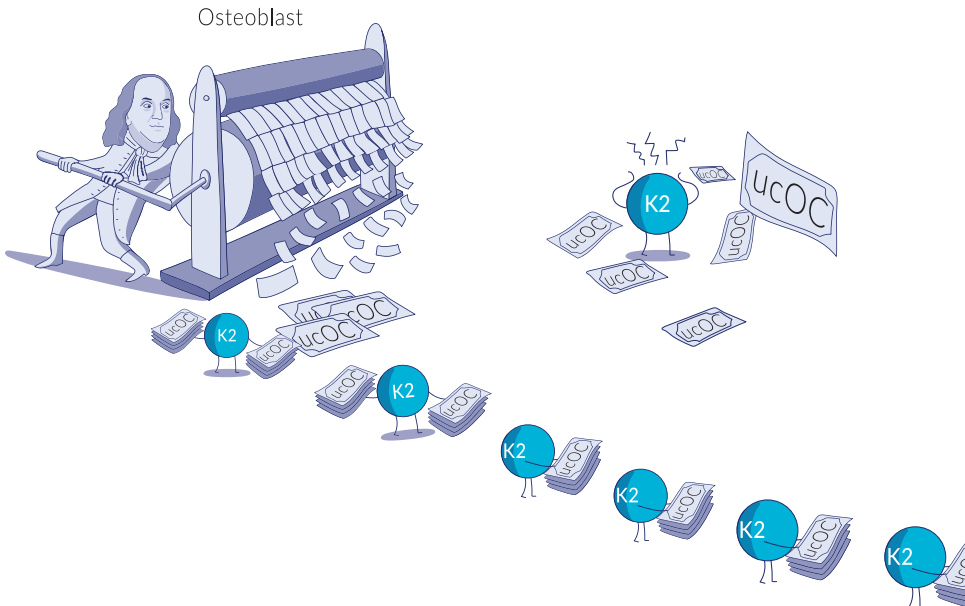
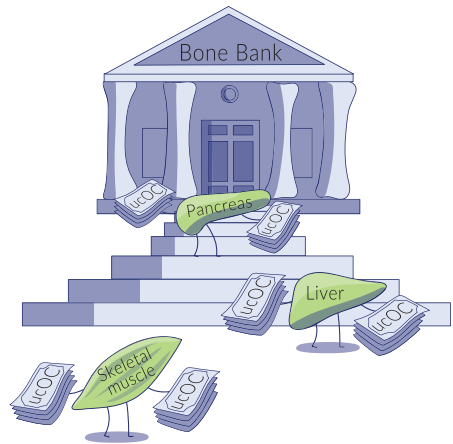
While a carboxylated osteocalcin deficiency may not impact bone mineral density, it might affect the bone's ability to withstand force and pressure, increasing the risk of fractures. It's like comparing two concrete bridges: one built with reinforced concrete versus one with no steel bars. While they may look the same and have the same mass, the one built with reinforced concrete will be able to withstand more weight-bearing loads.

Hormonal and metabolic health

Osteocalcin-lacking mice suffer other health problems. They are overweight and hyperglycemic, due to their poor glucose tolerance, insulin levels and insulin sensitivity. Males have poor fertility, shown by lower testosterone levels and lighter weighing reproductive organs. Behavioural testing showed increased behaviours linked to anxiety and depression. Many of these symptoms have been observed in cross-sectional studies in humans, with significantly reduced blood osteocalcin levels reported in populations like pre-diabetics, untreated diabetics and obese children.

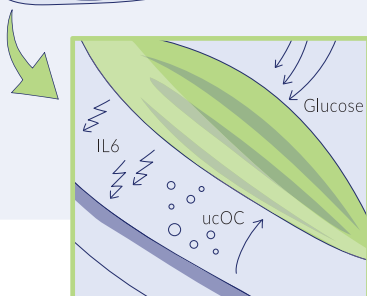
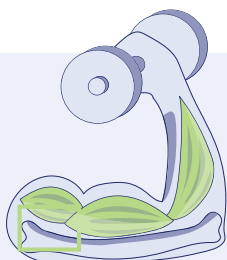
Our bones produce, store, and supply the osteocalcin needed for these hormonal and metabolic functions. When needed, bone cells called osteoclasts decarboxylate and release stored osteocalcin from the bone into the blood. From there,

this undercarboxylated-osteocalcin can travel to and influence different tissues in the body. Without vitamin K2 to activate and add osteocalcin to the bone matrix, there would be no store of osteocalcin for our body to draw upon.



Exercise and osteocalcin

When we exercise, our muscles secrete an inflammatory hormone called interleukin-6 (IL-6), which stimulates the decarboxylation and release of osteocalcin from our bones. This osteocalcin circulates to the skeletal muscles and increases the uptake of glucose and fatty acids, improving energy utilization, insulin sensitivity and muscle strength.



Matrix Gla protein (MGP) and calcium

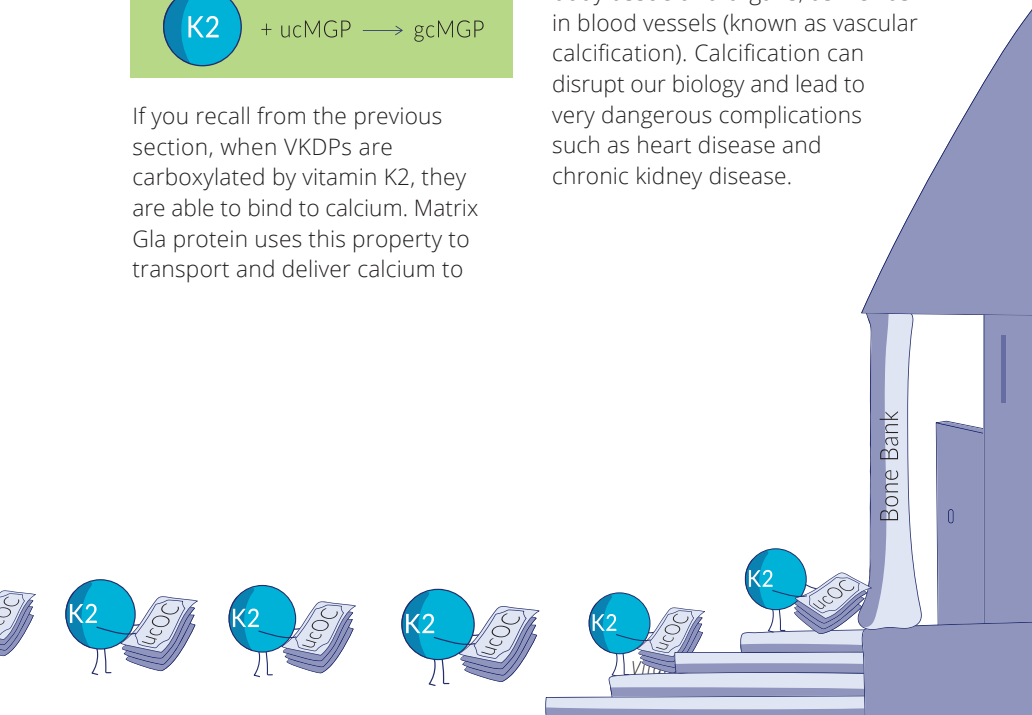
Another well-studied VKDP is matrix Gla protein (MGP). MGP is found throughout the body in vascular smooth muscle cells, soft tissues, and bone cartilage.



If you recall from the previous section, when VKDPs are carboxylated by vitamin K2, they are able to bind to calcium. Matrix Gla protein uses this property to transport and deliver calcium to

where it is needed, like the bone matrix and teeth where roughly 99% of all body calcium is stored.

This binding also prevents unwanted calcification - calcium buildup in soft body tissue and organs, as well as in blood vessels (known as vascular calcification). Calcification can disrupt our biology and lead to very dangerous complications such as heart disease and chronic kidney disease.



The dangers of calcium salts and tissue calcification

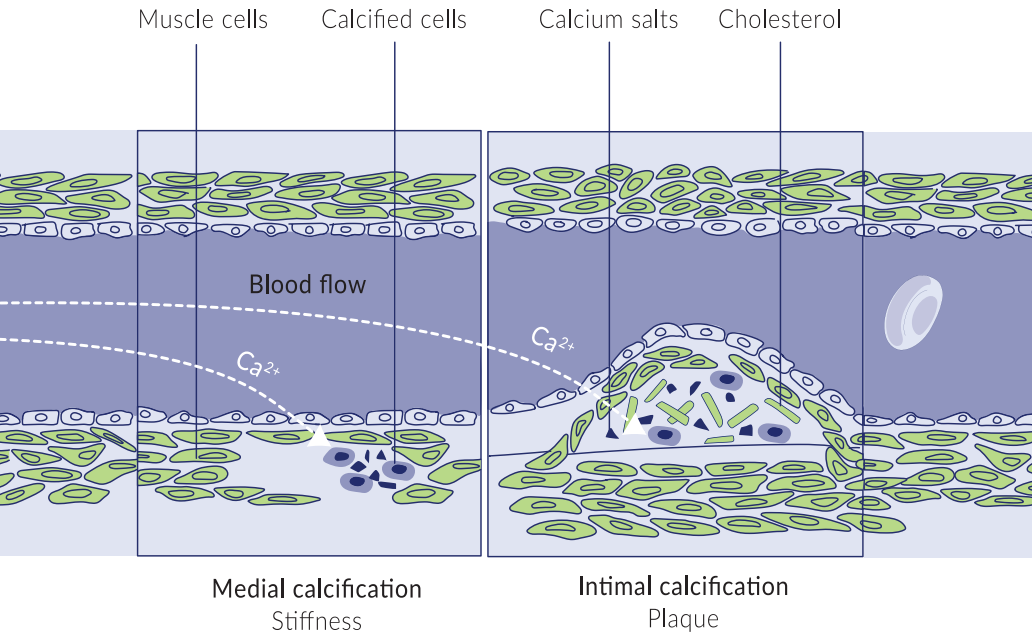
Calcium ions are very reactive. When dissolved in blood, calcium ions can react with phosphates to form calcium salts. With sufficient numbers and size, calcium salts can harmfully accumulate on soft tissues. For example, calcium salts can accumulate in the kidneys, forming kidney stones.

Calcium salts can also accumulate inside blood vessels. This is known as vascular calcification. Calcium can accumulate in and harden the elastic muscle cells of arteries, causing arterial stiffness. Research actually shows that these muscle cells essentially transform into

chondrocyte-like bone cells!
Not ideal for blood flow.

Also, along the inside (intimal) layer of these blood vessels, deposits of calcium salts can accumulate. Excess calcium salt circulation, along with cholesterol, can lead to atherosclerotic plaques and clogged arteries, severely blocking blood flow. Indeed, coronary artery calcification is an independent predictor of cardiovascular disease.

Calcification is not limited to the kidney and blood vessels. Since calcium is found in every cell, these accumulations could occur almost

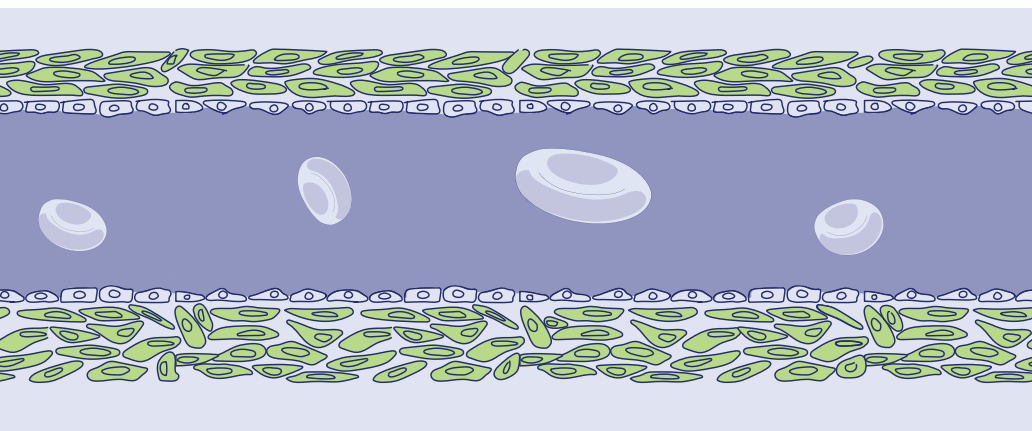


anywhere in the body, including joints, tendons, muscles, organs and even the brain. This is why many organs in the body produce matrix Gla proteins...and vitamin K2 to activate them.

Vitamin K2 carboxylated MGP prevents these salts from forming by binding calcium ions in the bloodstream. Calcium bound to MGP is unable to interact and form salts with phosphorus, preventing unwanted mineralization.

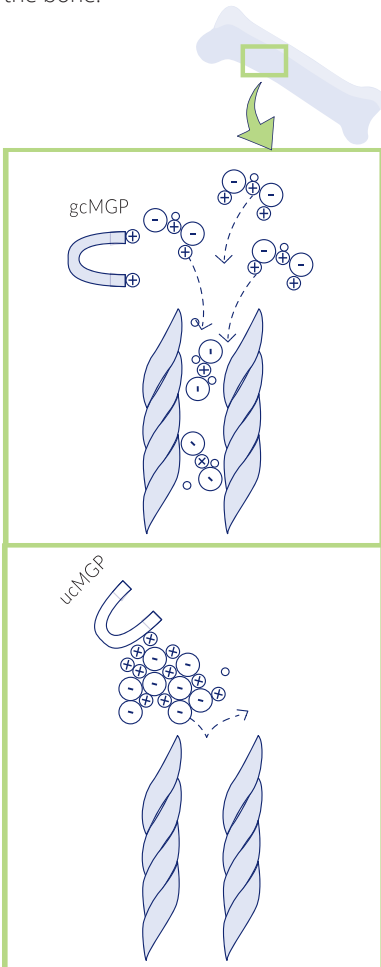
The relationship between vitamin K2 and vascular calcification has been shown in several studies. The previously mentioned Rotterdam

study showed that those who had the highest intake of vitamin K2 supplementation over a span of 7-10 years were 52% less likely to suffer arterial calcification. Another cohort study with 16,057 women suggested that for every 10mcg of K2 consumed per day, the risk of coronary heart disease was reduced by 9.1%. In healthy, postmenopausal women, there was an association between undercarboxylated-MGP and coronary artery calcification. Similar observations were made between vitamin K deficiencies and patients with chronic kidney disease. Vitamin K2 supplementation in hemodialysis patients decreased inactive MGP in the blood.



Calcium salts and bone mineralization

The formation of calcium salts can also impede needed mineralization of bones and teeth. Calcium-phosphate salts that are too large are unable to pass between proteins that make up the bone matrix. Activated MGP, by preventing the formation of calcium salts, allows calcium to penetrate the bone matrix and properly mineralize the bone.



Carboxylated MGP keeps calcium salts small, so they can pass through the bone matrix.

MGP prevents cartilage growth plates in the bone from prematurely calcifying

Childhood and adolescence are both periods of intense skeletal bone growth. For bones to lengthen and grow, cartilage at the growth plates of bones produces new cartilage that then calcifies and becomes bone. Once growth is complete, the cartilage in the growth plate calcifies.

This suggests that K2 is crucial for growing children and adolescents.

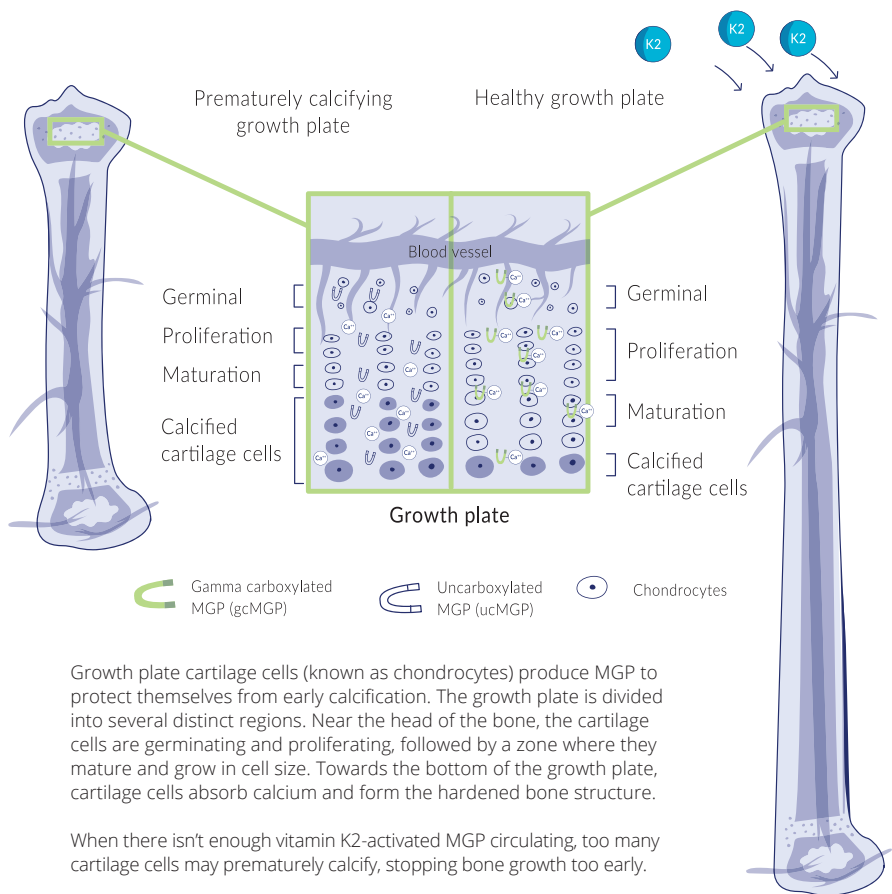
Other VKDPs

Besides the above, there are several more vitamin K-dependent proteins that still need to be more fully studied. They include Gla-rich protein (GRP) which might act as an anti-inflammatory and also inhibit calcification, periostin which may be involved in tissue regeneration and healing, and growth arrest-specific protein 6 (Gas6) thought to be involved with cell proliferation.

There are four more vitamin K-dependent proteins whose functions are still yet undiscovered. And more VKDPs are yet to be discovered!

Why take vitamin D3 and vitamin K2 together for bone health?

Many people know that vitamin D3 is essential for building and maintaining a healthy skeleton. Vitamin D3, after all, is essential for absorbing dietary calcium in the intestinal tract. Vitamin K2, by activating MGP, ensures that calcium traveling in the bloodstream reaches the bone and is properly incorporated into the bone matrix.



List of VKDPs

Clotting Factors - Factor II (prothrombin), Factor VII, Factor IX, Factor X

Circulating anti-coagulants - Protein C, Protein S, Protein Z

Bone Metabolism - Osteocalcin (OC) or Bone GLA protein (BGP), Matrix Gla-protein (MGP), Periostin, Periostin-like factor (PLF), Gla-rich protein (GRP)

Vascular biology - Gas6 (growth arrest specific gene 6 protein)

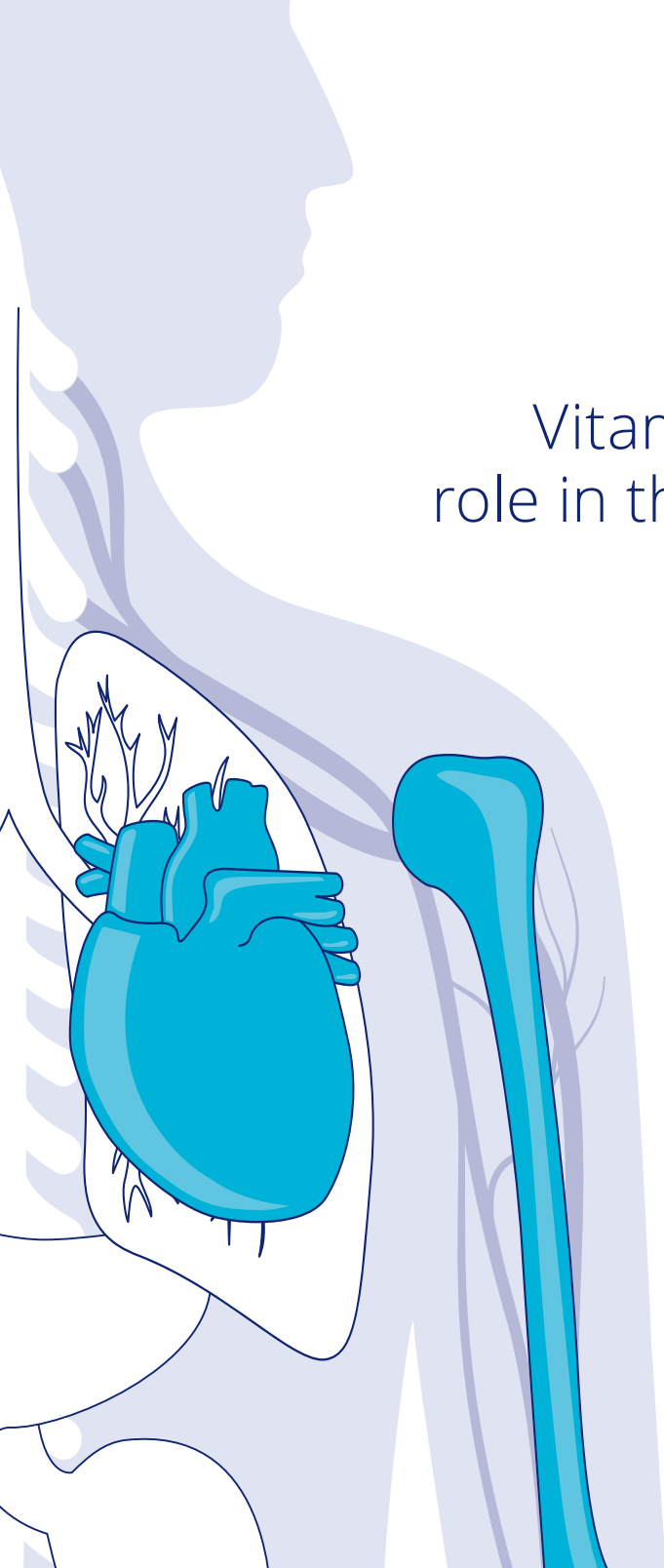
Functions not yet discovered! -

Proline-rich γ -carboxyglutamyl protein 1 (PRGP1), Proline-rich γ -carboxyglutamyl protein 2 (PRGP2), Transmembrane γ -carboxy glutamyl protein 3 (TMG3), Transmembrane γ -carboxy glutamyl protein 4 (TMG4)

Vitamin K2 and postmenopausal women

Several studies have demonstrated that vitamin K2 supplementation increases the activation of osteocalcin and MGP. In a study of 244 healthy postmenopausal women, taking 180mcg of MK-7 vitamin K2 daily for three years limited the age-related declines in bone mineral density and bone strength in the lumbar spine and femoral neck. Reduced loss of vertebral height in the lower chest region was also observed. Results also showed a significant decrease in arterial stiffness.

Vitamin K2's role in the body

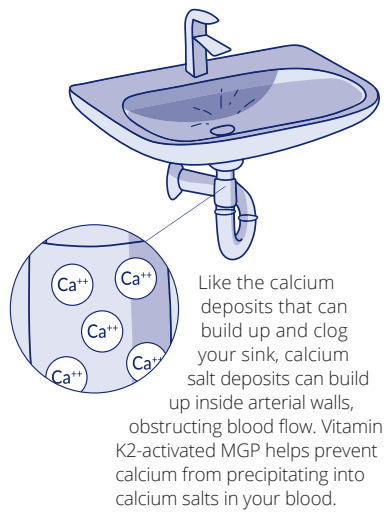


In the previous section, we explored the fundamental biology behind vitamin K2 and vitamin K2-dependent proteins in the body. When we take a step back, it's obvious that vitamin K2 is involved in a staggering number of functions and conditions. We've only just begun to understand the different ways vitamin K2 can help us. Here is a brief summary of functions and conditions that vitamin K2 is involved in.

Bone health

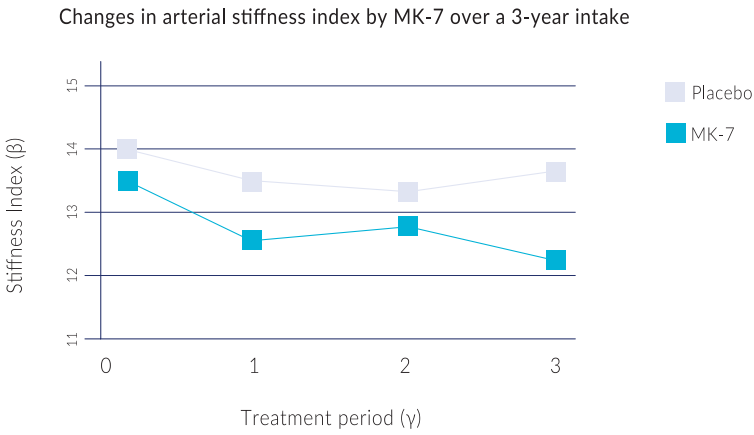
Vitamin K2 improves mineralization and metabolism in bones. It activates matrix Gla protein, which is responsible for delivering dietary calcium to the bone and integrating it into the bone matrix. It also activates osteocalcin which helps to form collagen fibril bands in the bone. These bands help to absorb tension and stress on the bone, improving fracture resistance.

obstructing blood flow. Coronary artery calcification is an independent predictor of cardiovascular disease.



Cardiovascular health

Vitamin K2 activates matrix Gla protein (MGP) in the blood which inhibits calcification of arteries and other soft tissues. Vascular calcification reduces the elasticity of blood vessels, resulting in arterial stiffness. It can also lead to calcium plaque buildup further



Calcium paradox: linking bone and cardiovascular health

Vitamin K2 deficiency can explain why high intakes of dietary calcium can still lead to poor bone mineral density, as well as cause arterial calcification. Without vitamin K2 to activate the calcium-transporting matrix Gla protein, dietary calcium cannot properly mineralize the bone and instead builds up in the soft tissues of the blood vessels.

It explains why osteoporosis sufferers are also more likely to exhibit atherosclerotic calcification while those with atherosclerosis (arterial deposits/plaque) are more likely to have weaker, brittle bones.

Studies on the effect of vitamin K2 MK-7 on cardiovascular health show a significant reduction in arterial stiffness and slower progression of calcification. As mentioned above in the Knapen et al. study, supplementation with 180mcg of MK-7 over a 3 year period, revealed a significantly improved stiffness index and MGP activation among healthy postmenopausal women.

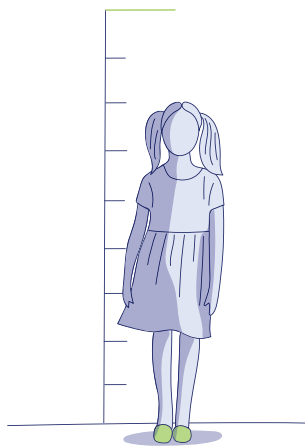
Evidence linking K2 to cardiovascular health is only growing. One study in 2016 looked at the effect various factors played in cardiovascular disease across 168 countries. They found that vitamin K2 deficiency was linked to early cardiovascular disease mortality - even to the same degree that tobacco use is.

Dental health

Like our bones, our teeth need vitamin K2 to support mineralization and prevent tooth decay. Odontoblasts, which line the dentin layer just underneath the enamel of teeth, produce osteocalcin. This osteocalcin needs to be activated by vitamin K2 before it can incorporate calcium into the dentin matrix.

Incidentally, some of the highest amounts of vitamin K2 in the body are found in our saliva. It has been observed that K2 has antimicrobial effects and reduces the number of cavity-causing bacteria, which helps to prevent tooth decay.

Child and adolescent growth



Childhood and adolescence are both periods of intense skeletal growth. Bone development begins as early as six weeks after conception and continues well into adulthood. Peak bone mass (bone mineral density) is achieved sometime around the age of 20, before beginning a natural and steady decline. Vitamin K2 is important for incorporating calcium properly into quickly developing bone structure.

Vitamin K2 activated matrix Gla protein is also needed to protect the cartilage in the growth plates of the bones from prematurely calcifying. This cartilage is essential for the bones to grow longer. If this cartilage calcifies too soon, child growth may be stunted.



Studies have shown that supplementing with vitamin K during childhood years can have a significant impact on bone mineral density and decreased bone turnover. In one particular 2009 study, pre-pubertal children that supplemented with 45 mcg of K2 MK-7 over 8 weeks, were found to have

increased concentrations of both circulating MK-7 and active, carboxylated osteocalcin.

Pregnancy

Research indicates that during pregnancy, vitamin K2 is particularly important for both the mother and the fetus.

Pregnant women can become calcium deficient because of substantial skeletal remodeling to prepare for birth and the baby's high demand for skeletal formation. In extreme cases, this can result in pregnancy-associated osteoporosis, a condition characterized by severe pain from vertebral fractures. K2 supplementation has been shown to relieve this pain and improve bone health in expectant mothers.

Vitamin K2 is also needed by the infant to support skeletal development both during gestation and after birth. A K2 deficiency during gestation can be detrimental for future bone health.

After birth, infants are also at risk of vitamin K2 deficiency as the levels of vitamin K in breast milk are typically very low. Lactating mothers can increase the levels of vitamin K2 in their breast milk with supplementation. The transfer seems to be successful as the breastfed children in these studies also had elevated vitamin K levels in their blood. It is, however, recommended that additional K2 supplementation in infants be considered as transfer adequacy of K2 from breastmilk is still unclear.

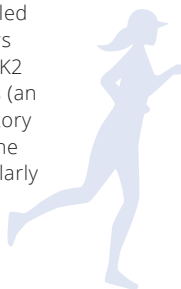
Blood sugar balance

Vitamin K2 helps to activate and buildup stores of carboxylated osteocalcin in the bone. When needed, this supply of osteocalcin is regularly decarboxylated and released into the bloodstream, where it is used by the pancreas to increase insulin production, and by the rest of the body to improve insulin sensitivity and glucose metabolism.

Studies show that mice who lack the osteocalcin producing gene suffer from poor glucose tolerance, insulin levels and insulin sensitivity. Pre-diabetics and untreated diabetics have decreased levels of serum osteocalcin.

Inflammation

K2 has been shown to fight inflammation by inhibiting pro-inflammatory markers produced by white blood cells called monocytes. Researchers looking at the effect of K2 on rheumatoid arthritis (an autoimmune inflammatory condition that affects the entire body but particularly the joints) found that supplementation with K2 lowered levels of inflammatory markers.



Athletic performance

Vitamin K2's effects on our glucose metabolism and cardiovascular system may help with athletic performance. An 8-week, double-blind, placebo trial with 26 male and female athletes showed 12% increase in maximal cardiac output after daily supplementation with the MK-7 form of vitamin K2.

Male fertility

Osteocalcin released from the bone is thought to upregulate the synthesis of enzymes needed for the biosynthesis of testosterone, increasing male fertility. Osteocalcin deficient male mice exhibited poor fertility, lower testosterone levels and lighter weighing reproductive organs than their wild counterparts.

Kidney health

K2 is key in controlling vascular calcification, which is a common condition and risk factor for people who suffer from chronic kidney disease (CKD). Indirect evidence suggests that vitamin K2 supplementation may reverse vascular calcifications in CKD patients. A four-week supplementation trial with MK-7 vitamin K2 showed decreased inactive forms of matrix Gla protein, possibly reversing calcification.

Another randomized controlled trial found that vitamin K supplementation, in conjunction with vitamin D supplementation, reduced the progression of atherosclerosis in patients with CKD significantly more than vitamin D supplementation alone.

Brain health



Vitamin K2 paired with calcification-inhibiting matrix Gla protein may help prevent strokes and other blood obstructions to the brain. One

study suggests that osteocalcin crosses the blood-brain barrier to act in the brainstem, midbrain and hippocampus, influencing the synthesis of monoamine neurotransmitters. Other studies show that vitamin K2 dependent proteins might act as antioxidants to prevent oxidative stress, which can cause nerve cell and brain damage.

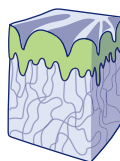
Prostate health

Benign Prostate Hyperplasia (BPH) - the enlargement of the prostate gland - is pervasive among older men in modern society, but its root cause is still unknown. However, recent research discovered that BPH does not occur without a varicocele - a twisted and swollen varicose vein found in the scrotum. The swelling causes blood from the testes to backflow into the prostate gland. The high testosterone levels in this blood may lead to enlargement of the prostate.

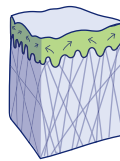
How does vitamin K2 factor in? Varicose veins have been characterized by high levels of undercarboxylated-MGP, which suggests that a vitamin K2 deficiency might be a factor in varicose veins and varicocele. Supplementing with K2 may prove beneficial for BPH prevention in aging men.

Skin and aging

Some of the latest research suggests that vitamin K2 plays a role in protecting skin elasticity. In the same way that K2 prevents calcification in other soft tissues, it prevents the calcification of our skin's elastin, the protein that gives skin its elasticity and smooths out lines and wrinkles.



**calcified
elastin**



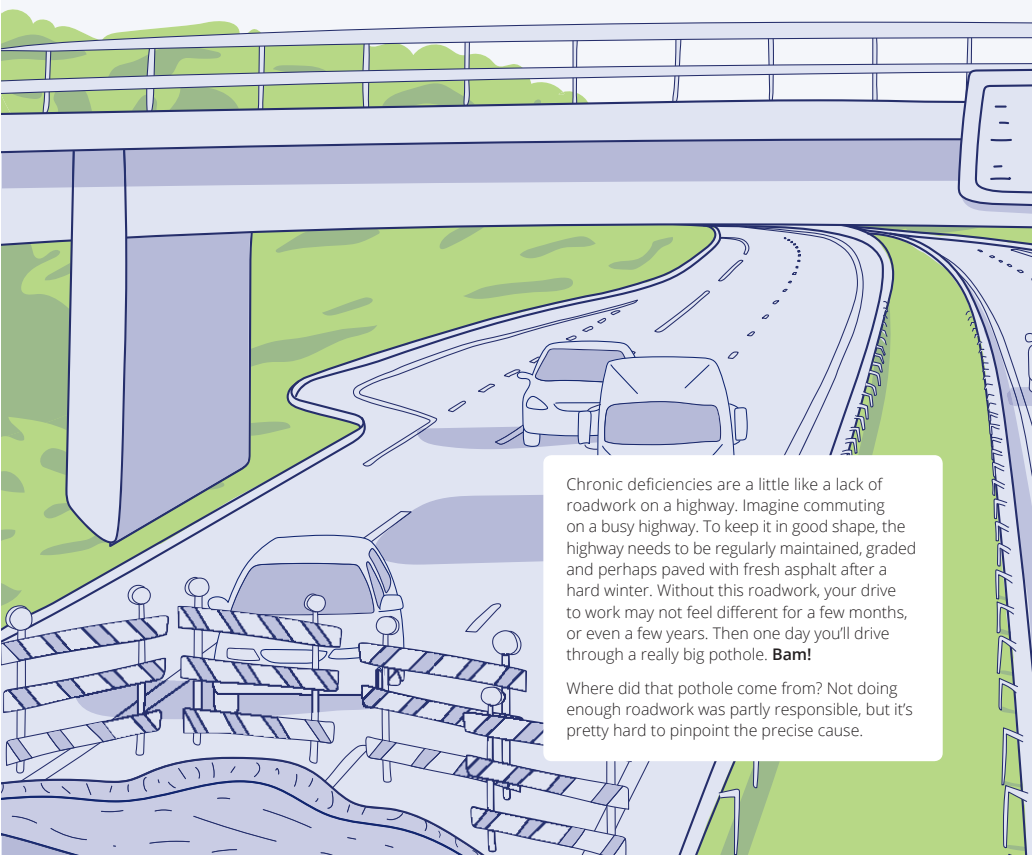
**non-calcified
elastin**

Skin cells release matrix-GLA protein (activated by vitamin K2) to prevent calcification of elastin in the skin. Low K2-MGP may result in premature aging and wrinkles.

Can't get enough of a good thing

For a long time after the discovery of vitamin K, we thought that deficiencies were rare and obvious. We were only partly right.

Now armed with a better understanding of the differences between K1 and K2, there is growing concern that a K2 deficiency is widespread and that the symptoms of this deficiency are not obvious and pass unnoticed.



Chronic deficiencies are a little like a lack of roadwork on a highway. Imagine commuting on a busy highway. To keep it in good shape, the highway needs to be regularly maintained, graded and perhaps paved with fresh asphalt after a hard winter. Without this roadwork, your drive to work may not feel different for a few months, or even a few years. Then one day you'll drive through a really big pothole. **Bam!**

Where did that pothole come from? Not doing enough roadwork was partly responsible, but it's pretty hard to pinpoint the precise cause.

K2: the widespread, silent deficiency

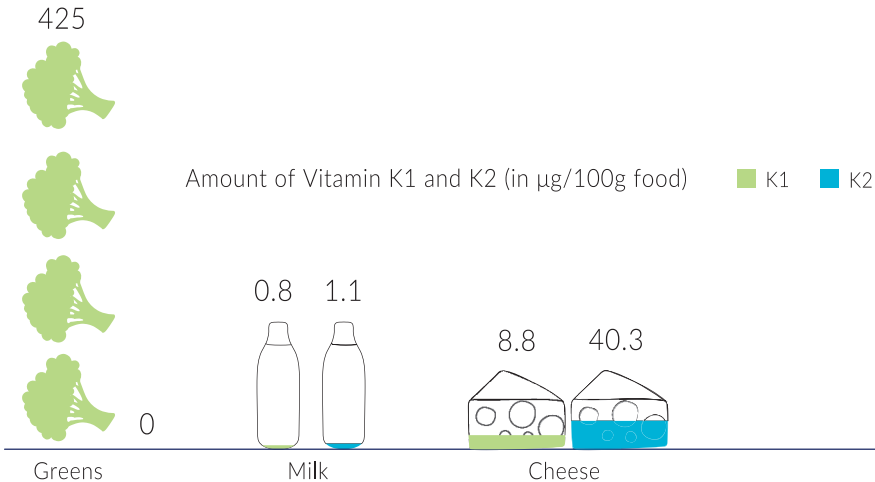
Unlike K1's direct impact on blood clotting, a K2 deficiency may not have any acute signs. Instead, K2's role in our biology is long-term and systemic. A chronic deficiency of K2 may take years to manifest - years before we see decay to our cardiovascular or skeletal health in the form of chronic diseases or fractures.

Based on this measurement, they found that 31% of the total population had functional vitamin K insufficiency, with significantly higher levels among the elderly and subjects with hypertension, type 2 diabetes, chronic kidney disease and cardiovascular disease.

We may be sub-clinically deficient as early as childhood!

Another study tested vitamin K2 status and supplementation with a group of 110 healthy participants, 42 children and 68 adults. Analyzing 896 blood samples for undercarboxylated VKDPs osteocalcin and MGP, they found that children and adults over the age of 40 show the largest K2 deficiency.

What's causing this widespread deficiency?



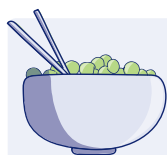
It's missing in our diets.

Unlike vitamin K1, which is easily found in green leafy vegetables and plant oils, vitamin K2 is microbial in origin and is much harder to find in our diets.

If you recall the expeditions of Dr. Weston Price, he noted that many pre-industrial societies had traditional foods that were rich in

fat-soluble nutrients. Traditional foods like fish eggs, butterfat from grass-fed cows, cured meats, kefir, sauerkraut, organ meats, and aged cheeses. Foods we now understand to be rich in vitamin K2.

Foods that are no longer very common in the modern North American diet.



Natto: the fermented soy superfood

Today's Japanese palate still features many popular fermented foods, such as pickled vegetables (tsukemono), pickled plums (umeboshi), miso soup and tempeh. However, one dish stands out for being the highest dietary source of vitamin K2 MK-7 in any food: natto.

Dating back to 1000AD, natto is a traditional breakfast dish made from fermented soybeans. The natto bacteria used in this fermentation process is responsible for producing the high concentrations of K2. 100 grams of traditional natto may contain as much as 950mcg of K2 MK-7! You can obtain all the K2 you need eating 15-20 grams of natto daily.

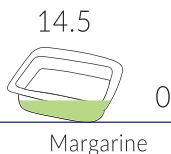
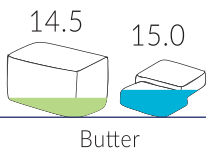
Unfortunately, natto has a reputation for being an acquired taste and is virtually not eaten regularly outside of Japan. It has a pungent odour, sticky to handle, and can be a little slimy. However, given its K2 content, we recommend you at least give it a try!

After all, how often do you tuck into hearty servings of goose liver pâté, brie, gouda or prosciutto - fermented foods that used to be cornerstones of a healthy European diet?

It's easy to forget that our diets have changed tremendously in the past century. And as a result of these changes, we are consuming much less K2 than our grandparents did.

Refrigeration and other miracles of modern food preservation

A big reason why we don't eat as many fermented, cured or pickled foods is that we no longer need to cure, ferment or pickle to prevent foods from spoiling.



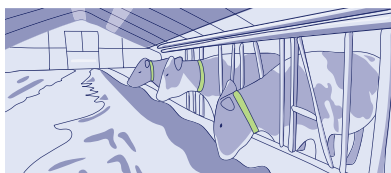
Modern food preservation methods like refrigeration, canning and pasteurization changed our diets mostly for the better. It increased our access to fresh foods year-round, added a great variety to our diet and reduced food prices.

Unfortunately, as our palates changed to favour the new flavours of refrigerated ingredients, K2 rich traditional food sources from traditional preservation methods like fermentation became less popular.

Industrial farming practices

Traditionally good animal sources of vitamin K2 MK-4, like dark meat, butter and eggs, are depleted of K2 today thanks to industrial farming practices.

Dairy cattle, hens and other livestock produce K2 by converting the K1 they consume in fresh plant sources and grass. That's why the best K2 sources of eggs, dairy and meat come from animals that are grass-fed, free-range or pasture raised - free to eat their natural diet.



On factory farms, animals are primarily grain-fed. Without their K1 supply, they do not produce K2 in the quantities we expect.

Common drugs interfere with K vitamins.

Another big concern is the impact common medications have on the absorption, metabolism and use of vitamin K in the body. While not all the mechanisms of interference are known, many studies have linked prescription and over-the-counter medications to both lower K1 and K2 status.



Coumarin anti-coagulants

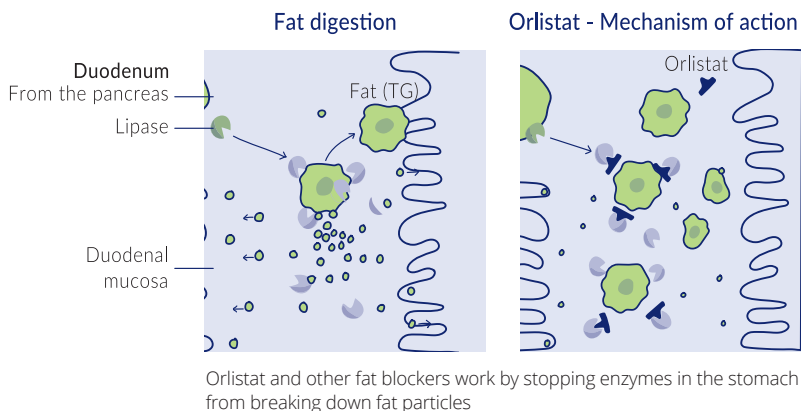
Some drugs inhibit vitamin K by design. Coumarin anticoagulants like warfarin interfere with the body's ability to recycle vitamin K in order to prevent the activation of VKDP clotting factors. Unfortunately, the indiscriminate interference targets both vitamins K1 and K2, preventing the latter from activating other VKDPs essential to our health.

Fat-blocking medications

Because K vitamins are fat-soluble, they require fats for absorption and transport through the body. That's why we absorb less than 20% of K1 from green vegetables (and why adding a good healthy fat like olive oil to your vegetables can help improve that absorption!). Many fat-blocking medications, such as orlistat, interfere with fat absorption and prevent us from absorbing vitamin K in the gut.

Antibiotics

It is thought that our gut bacteria are involved in vitamin K absorption. Broad-spectrum antibiotics may interfere with this process.



Statin medications

Ironically, many medications taken for heart disease jeopardize vitamin K2 necessary for good cardiovascular health. These medications typically target cholesterol in the liver. For example, statins block an enzyme in the liver responsible for producing cholesterol. Bile acid sequestrants force the liver to divert more cholesterol to replace lost bile acid.

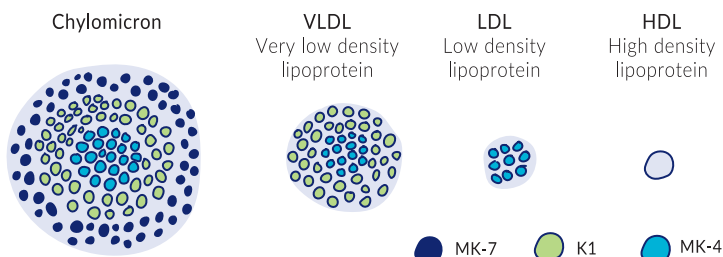
What does cholesterol have to do with vitamin K2?

Since vitamin K is fat-soluble, it needs to travel through the aqueous environment of our bloodstream in vessels called lipoproteins. These

lipoproteins carry vitamin K to soft tissues and bones all across the body. Lipoproteins are made in the liver using cholesterol.

Not enough cholesterol, results in not enough vitamin K2 movement in the body. The studies back this up, with research suggesting that statin drugs inhibit the formation of vitamin K2.

Given the number of drugs Canadians are taking today, vitamin K2 deficiencies due to medication alone could be widespread. Statistics Canada found that 1 in 10 Canadian adults are taking statins.



Since all K vitamins are fat-soluble, they need fat-friendly lipoproteins to travel through the bloodstream and to different parts of the body

Am I getting enough vitamin K2?

At this point we know what it is, some of the complex roles it plays in the body, and even some of the reasons for why it's hard to obtain. All well and good. But what you really want to know is whether you're getting enough vitamin K2.

Well, what is enough?

This is a surprisingly difficult question.

One of the legacies of confusing K2 with K1 is that nutritional authorities still think of vitamin K as one ingredient. When you look up guidelines from agencies like Health Canada, the US Institute of Medicine and the European Food Safety Authority, you will only find official recommendations on vitamin K as a whole, not vitamin K2.

By treating K vitamins as a single nutrient, it's hard to calculate how much is consumed and absorbed into the body, how much vitamin K is needed in different parts of the body, and how to measure vitamin K status as a whole. With all this confusion, it's easy to see why these groups struggled to establish recommended dietary allowances (RDA) for vitamin K, only setting adequate intake (AI) levels.

Age	Men	Women	Pregnant
0 to 6 mo	2.0 mcg	2.0 mcg	
7-12 mo	2.5 mcg	2.0 mcg	
1-3 y	30 mcgs	30 mcg	
4-8 y	55 mcg	55 mcg	
9-13 y	60 mcg	60 mcg	
14-18 y	75 mcg	75 mcg	75 mcg
19+ y	120 mcg	90 mcg	90 mcg

Adequate Intakes (AIs) for Vitamin K

These Adequate Intakes are still based mostly on our understanding of vitamin K1. A vitamin K deficiency is still clinically characterized only by a bleeding tendency and poor blood coagulation.

Recommended Dietary Allowance (RDA) vs Adequate Intake (AI)

RDA is the average daily level of intake that's sufficient to meet the nutritional requirement for 97-98% of all individuals.

AI is a level assumed to ensure nutritional adequacy, established only when evidence is considered insufficient to set an RDA.

If we look at the current body of vitamin K2 research, we can see that a wide range of doses have been administered.

Some studies have administered pharmacological doses of K2 as high as 45 milligrams of vitamin K2 MK-4 per day. While high dose studies demonstrate the safety of consuming K2 at high doses, they don't tell us how much we ought to take. They show us safety only, not efficacy.

Other studies have used vitamin K2 MK-7 doses between 90 and 480mcg. Most of the health benefits seem to come from the first 100 micrograms, but higher doses have shown improvements in the form of increased carboxylated VKDPs.

If you're in great health and taking at least 100mcg of vitamin K2 daily, you probably have nothing to worry about. But if you think there's room to improve on any of the health categories we discussed earlier, consider a higher intake. Your vitamin K2 status is definitely something worth discussing with your physician or naturopathic doctor.

Can I test my vitamin K2 levels?

One of the reasons why it's so hard to determine a recommended dietary intake for vitamin K2 is that there's no standard way to test for vitamin K2 status.

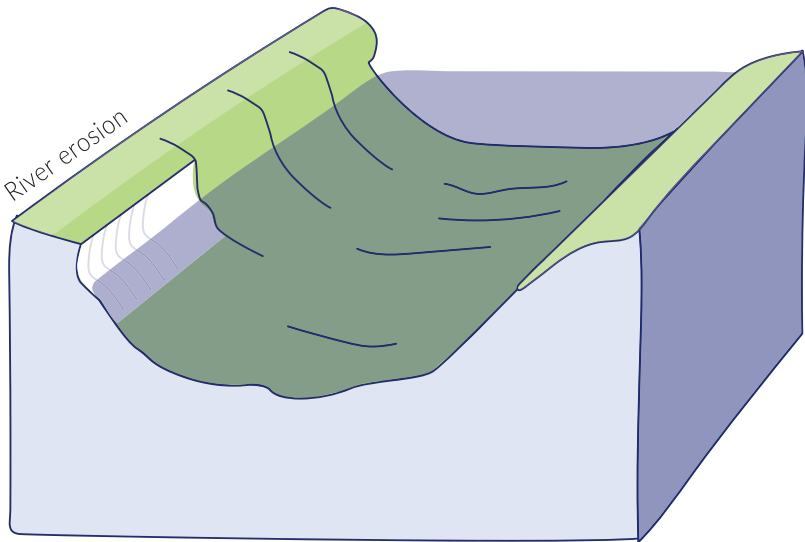
We don't know enough about how different levels of vitamin K2 in the body interact with each other. What does it mean if we measure vitamin K2 in our blood versus in the liver? Or in tissues versus the bone? Does a low level in one part of the body mean a low level of K2 everywhere else in the body?

And since we do not store vitamin K for long periods in our body, a vitamin K blood test would only



measure our recent intake rather than a long-term nutritional status.

Researchers currently assess K2 status in subjects by measuring the carboxylation status of vitamin K-dependent proteins like osteocalcin and MGP. These tests are shown to respond to the supplementation and depletion of vitamin K2 in the body. For example, a high level of undercarboxylated osteocalcin in the bone or



Measuring vitamin K2 status by measuring the carboxylation status of VKDPs is akin to gauging the water flow of a river over time by measuring the erosion of a river bank. A highly eroded river bank may indicate a high volume of water. A high level of carboxylated VKDP may indicate good vitamin K2 status.

undercarboxylated MGP in the blood may indicate inadequate intake of K2 over time.

The most promising VKDP to measure is matrix Gla protein in the blood. Clotting factors in the liver are acted on by both vitamins K1 and K2. And we don't know enough about how our bones release undercarboxylated osteocalcin into the blood.

As of this writing, there's no publicly available tests for measuring undercarboxylated VKDPs. They are only available to researchers right now. But we are optimistic that this kind of testing will be available to you soon.

Can I have too much vitamin K2?

Doses of vitamin K2 many times higher than typical nutritional intake have been safely administered during large-scale trials. Plus, unlike other fat-soluble vitamins, K vitamins are quickly metabolized, used and expelled - the body does not accumulate large stores of K1 or K2.

Still, it's important to be careful not to take any supplements at

doses higher than what is known to be beneficial. Even if high doses are generally safe, they may have potential side effects that have not yet been studied.

If you are taking prescription medications like anticoagulants, definitely consult your physician or other healthcare practitioner about K2 doses. Blood thinners like warfarin and other 4-hydroxycoumarins work by inhibiting the action of vitamin K. Some studies show that small doses of K2 (up to 50 mcg) were

*Assessing vitamin K status, via circulating undercarboxylated MGP levels, has shown that some vitamin K deficiency or insufficiency has been seen in **97%** of older subjects in a mixed population.*

able to activate osteocalcin without countering the effects of warfarin.

The best recommendation is to consult with your healthcare practitioner before incorporating vitamin K2 into your daily regimen.

Am I at risk for a vitamin K2 deficiency?

Unlike vitamin K1 deficiency, identified by a bleeding tendency, there is no single sign or symptom that marks a vitamin K2 deficiency. However, certain conditions and risk factors when surveyed together, can provide a clearer picture about your vitamin K2 status.



Here's a checklist of symptoms and risk factors to help you figure out whether you're getting enough vitamin K2. Tick off the corresponding box for any statements that apply to you. Check this list every four months or so to see whether supplementation has improved your signs, symptoms and conditions.

Vitamin K2 status checklist

Baseline
Month 4
Month 8
Month 12

Risk Factors: Diet and Lifestyle				
Low animal and fermented food (sauerkraut, natto, miso) intake in diet				
Low fat diet				
History of bariatric surgery				
Risk Factors: Medications				
If you are taking...				
Antibiotics				
Coumarin anti-coagulants/blood thinners, such as Warfarin				
Anticonvulsants				
Statin medications				
Bile acid sequestrants				
Certain weight loss drugs, like Orlistat				
Risk Factors: Conditions				
Fat malabsorption disorders: cystic fibrosis, liver/biliary disease				
Celiac disease				
Inflammatory gut disorders: Crohn's and ulcerative colitis				
Intestinal hyperpermeability (Leaky gut syndrome)				

Baseline
Month 4
Month 8
Month 12

Signs & Symptoms				
Easy bruising or bleeding				
Frequent nosebleeds/bleeding gums				
GI tract bleeding (blood in urine, stool or vomit)				
Heavy, painful menstrual cycles				
Frequent fractures or broken bones				
Osteoporosis or osteopenia (bone density loss)				
Joint pain and inflammation (osteoarthritis)				
Heart disease (including chest pain, palpitations)				
Poor dental health				
Prediabetes				
Varicose veins				
Chronic kidney disease				
Signs of premature aging				

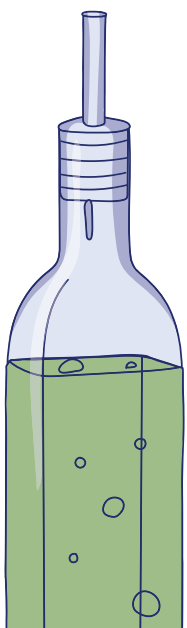
Don't forget to help your body's absorption.

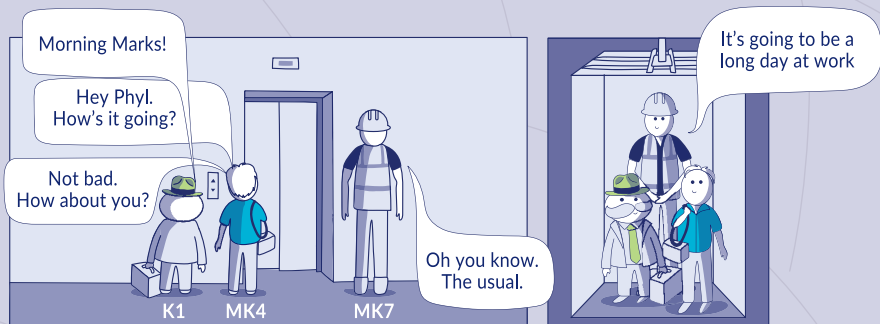
As vitamin K is a fat-soluble vitamin, taking a K2 supplement with dietary fat will improve absorption. Try to take K2 with a meal containing healthy fats like olive oil, butter, avocado and coconut oil.

You can also try to stack your K2 with other fat soluble vitamins. Emerging research shows the synergistic effects of all four fat-soluble vitamins A, D, E and K.

In particular, taking vitamin D with K2 ensures the best effect on bone and cardiovascular health. Vitamin D assists with absorbing calcium

from the intestinal tract. Without pairing it with K2 to activate matrix Gla protein, this additionally absorbed calcium may accumulate in soft tissue and arteries.





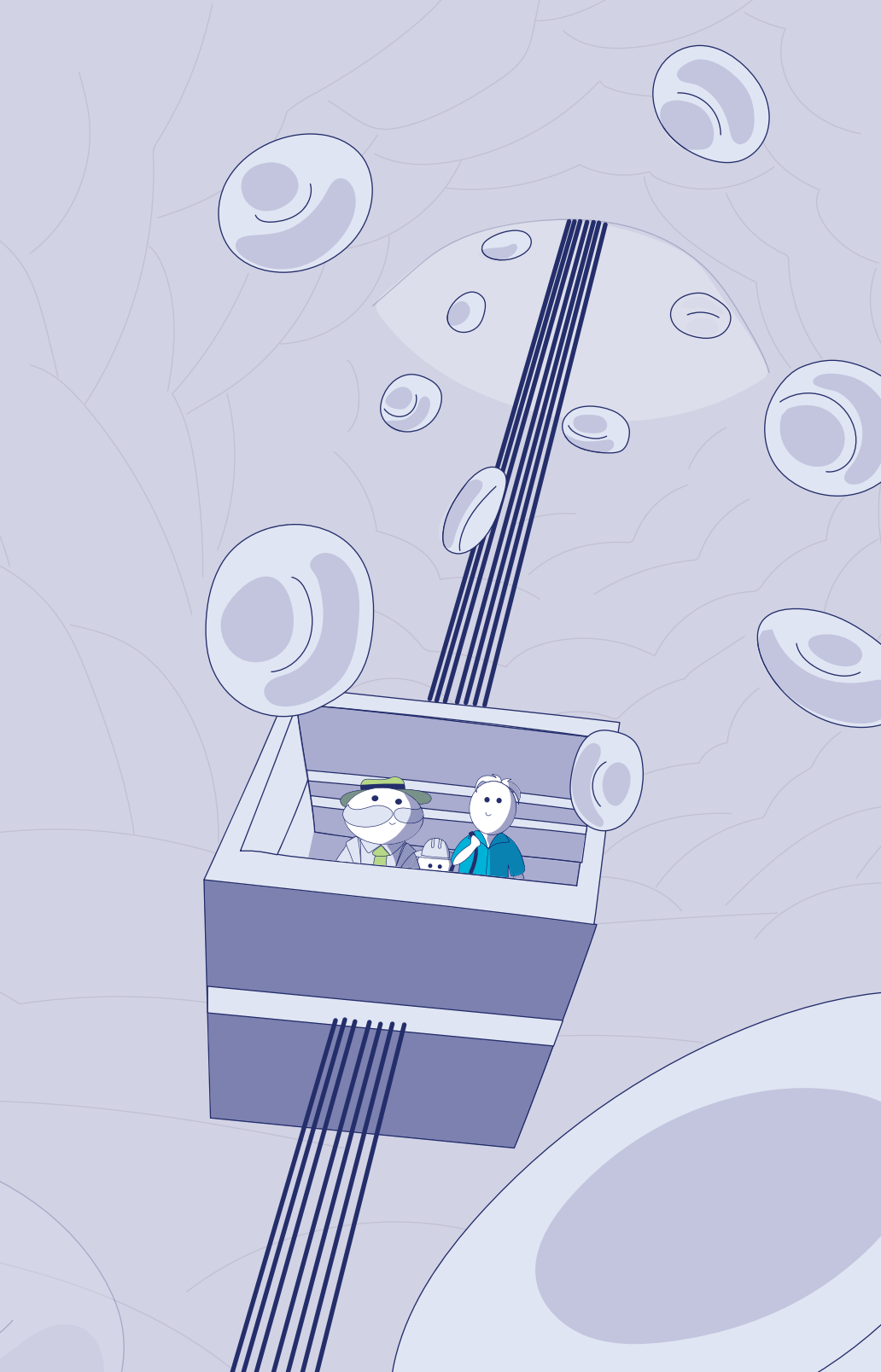
What form of vitamin K2 should I take?

Throughout this primer, we've discussed many differences between vitamin K1 and K2. We've also mentioned two common forms of vitamin K2 - MK-4 and MK-7. These three forms, vitamin K1, K2 MK-4 and K2 MK-7, are the most common kinds of vitamin K supplements on the market.

But which one is the best form to take?

Here's the short answer. Based on our latest understanding of vitamin K2 in the body with the latest research, the best form to supplement with is the **MK-7 form of vitamin K2**.

To understand why, let's revisit some of these differences.



Vitamin K1 vs K2 - different roles in the body

If you've read this far, you should have a good appreciation for how different vitamins K1 and K2 are. While vitamin K1's primary role is blood coagulation, vitamin K2 is better for general health, due to its ability to better activate vitamin K-dependent proteins like matrix Gla protein and osteocalcin throughout the body. This allows it to support a wide range of biological functions like bone building and cardiovascular health.

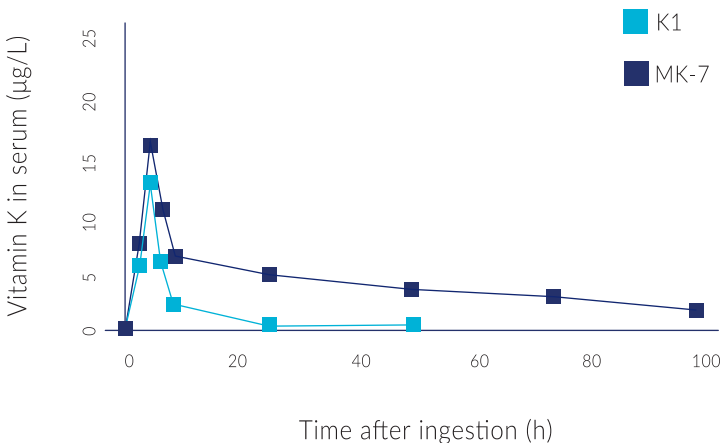
Research supports this difference in roles. For example in the large scale Rotterdam Study, despite K1 intakes eight times higher than K2, only K2 demonstrated an inverse correlation to cardiovascular disease risk and aortic calcification.

Vitamin K1 does have some effect on activating VKDPs like osteocalcin. However the big difference is in the doses required. Studies that show vitamin K1 affecting the

carboxylation of osteocalcin use doses in the range of 1 to 45mg per day, whereas MK-7 does the same at doses as low as 100 micrograms. At equal doses, MK-7 is three times better at carboxylating osteocalcin compared to K1.

Part of that reason is that K2 MK-7 has a much longer lifespan (or bioactivity) in the body than K1. Typically K2 MK-7 has a half-life of 72 hours. K1 only stays in circulation for a few hours before being flushed from the body.

Lastly, dietary sources of K2 are scarcer than that of K1. K1 is easily found in green leafy vegetables like kale, collard greens and spinach. Good dietary sources of K2 such as animal products from pasture-raised livestock and fermented foods are harder to include in meals on a regular basis. So most adults are not K1 deficient, but there is a higher risk of being K2 deficient.

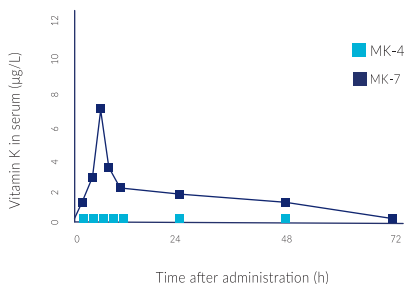


Vitamin K2 MK-4 vs MK-7

While MK-4 and MK-7 are both forms of vitamin K2, in terms of bioactivity and lifespan, MK-4 is more like K1 than it is like MK-7.

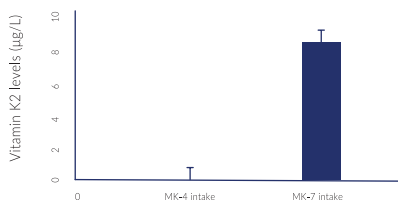
For one, MK-4 has an extremely short life-span. MK-7 can linger in the blood for days. MK-4? It has a half-life of only 1.5 hours.

In fact a 2012 Japanese dose-comparison study comparing MK-4 and MK-7 blood levels after ingestion, researchers had difficulty detecting any amount of MK-4 in blood serum at any time point during the test!



Single 420mcg dose of MK-4 or MK-7 was administered to healthy subjects with a standard breakfast. While MK-7 reached maximal serum levels 6 hours after intake and was detected up to 48 hours later, MK-4 was not detectable in blood serum of all subjects at any time point. (Sato 2012)

It seems like most of the MK-4 is taken up by our tissues quickly after consumption but does not circulate for long in the blood. This makes it difficult to build up and accumulate a stable level of vitamin K your blood. To get the same consistent level of a single dose of MK-7, you may need to supplement multiple times with MK-4.



Increased serum vitamin K2 levels in subjects after 7 days of consecutive administration (60 µg/day) (Sato 2012)

“Sure”, you might say, “but just because MK-4 is undetected in blood tests doesn’t mean it is less effective in the body.”

You would be absolutely right to question that. As we mentioned earlier, a vitamin K blood test would only measure recent intake rather than a long-term nutritional status. And we don’t know how long MK-4 is stored in tissues and other organs in the body. But we can test long-term nutritional status based on how well each form activates VKDPs in the body.

A 2005 Japanese study looked at this issue exactly, trying to determine the minimum effective dose of MK-4 for affecting levels of activated osteocalcin in blood. Researchers started by administering 500mcg per day of MK-4 over a period of 2 months. However, there was no effect on the status of osteocalcin carboxylation. Only after administering an intake of 1500mcg per day of MK-4 was there an observable improvement in carboxylation status. By contrast, MK-7 has been shown to carboxylate

osteocalcin with as little as a 45 to 90 mcg daily dose.

One of the main reasons that MK-7 circulates in the body longer than K1 or MK-4 is that it is more fat-soluble and therefore circulates in longer lasting low-density lipoproteins (LDL). LDL circulates in blood considerably longer than its bigger cousins like chylomicron and VLDL, which carry all three forms of K.

LDL transport may be the reason why MK-7 is so biologically effective at carboxylating osteocalcin in bone. It's been demonstrated that in cell cultures, osteoblasts readily absorb vitamin K from LDL fractions.

Are all MK-7s the same?

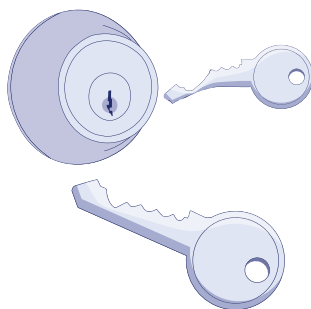
To complicate matters, even if a molecule has exactly the same atoms, they may be put together in different ways. This is called isomerism and happens all the time in nature. K2 MK-7 molecules commonly exhibit a type of isomerism called cis-trans isomerism.

Cis vs Trans Isomers

Cis-trans isomerism, also known as geometric isomerism, happens when functional groups in a molecule are rotated or bent into a different orientation. Shape is very important for coenzymes like vitamin K to work properly. Enzyme molecules like VKDPs are amino acid sequences folded into very specific shapes. In order for a coenzyme like vitamin

K2 to fit and interact with these molecules, they must maintain a specific shape.

If this shape is not quite right, it may slow down the activation of an enzyme or stop it completely. The easiest way to think of this is to imagine a lock and key. A straight key will fit the lock perfectly. A slightly bent key will need to be jiggled to get it to fit.



The type of K2 MK-7 isomer that activates VKDPs are trans-isomers. MK-7 cis-isomers have a bend in their carbon chain and do not readily activate VKDPs. Since trans-isomer MK-7 are more readily used by our body, they are considered more bioactive. Many K2 ingredients have a mixture of cis and trans isomers, depending on how well they are produced. You'll want to look for K2 supplements with a high percentage of trans-isomer MK-7, ideally 100%.

When we selected the K2 MK-7 to use in our products, we made sure to choose a form that was 100% all-trans. In fact, the ingredient we use is the United States Pharmacopeia (USP) standard, which is used to benchmark all K2 MK-7 ingredients for identity, quality and cis/trans purity!

Fermentation vs Organic Synthesis

There are two main ways to produce MK-7: fermentation and organic synthesis.

The fermentation method stimulates bacteria to produce MK-7 from a culture of soybean powder. After a period of time, this fermentation is filtered and the MK-7 is extracted and purified using solvents.

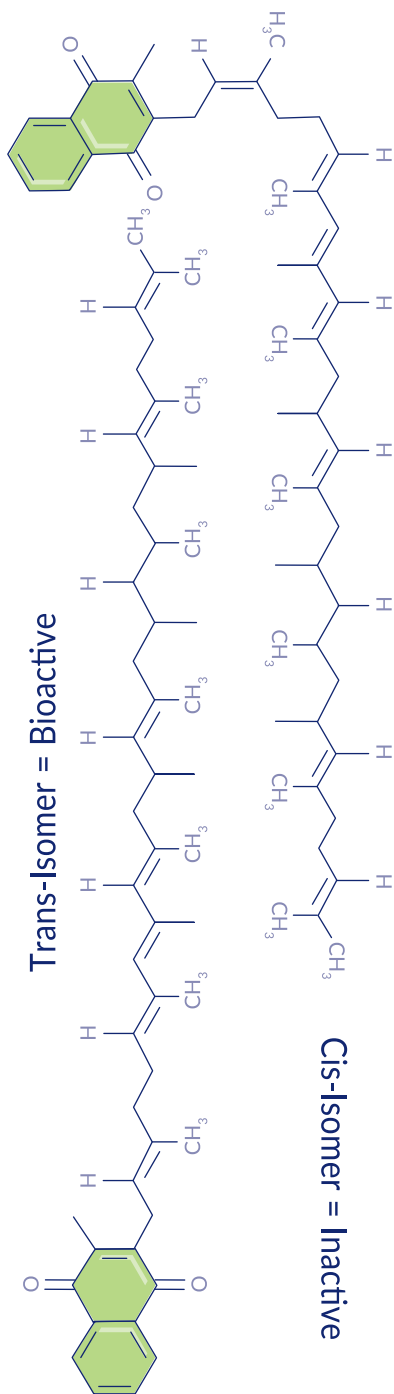
Organic synthesis is a proprietary method that begins with flower extracts farnesol and geraniol. Through a series of reactions it results in a pure all-trans form of menaquinone-7.

So, which method is better?

As long as the processes have high levels of quality control, both will result in a MK-7 molecule that is chemically identical. This was clinically studied. Two batches of all-trans MK-7, one produced by fermentation and the other by organic synthesis, had the same half-life and the same osteocalcin carboxylating activity in the body.

There are a few benefits of going with an organic synthesis produced MK-7. Those who have a sensitivity to soy may prefer to take an MK-7 produced by organic synthesis, as no soy is used. There's also a chance that fermented MK-7 may have a mixture of cis and trans if the purification step is not rigorous.

The primary thing to look for in your K2 MK-7 is that it has a high ratio of trans isomers.





CanPrev Vitamin K2: Designed to deliver more

By now, you've learned a little about why K2 is important for your health, how to best incorporate it into your life, and what forms make the most sense to you.

When designing our K2 supplements, we wanted to create a line that incorporated the latest understanding of science and research. Not only for delivering the best effective doses, but also in selecting the best forms to meet today's needs, and for optimizing the best bioactivity.

Good product design takes all of these challenges into account. We think we've done that with our K2.

CANPREV VITAMIN K2 MK-7



K2VITAL®

By Kappa Bioscience



Gluten Free



Dairy Free



Soy Free



Corn Free



GMO Free

K2 Drops & Softgels

CanPrev's K2 (K2VITAL®) offers a unique form of MK-7 that is derived from the organic synthesis of non-soy plant oils (geraniol and farnesol), yielding a pure, bio-active, stable and 100% trans form that is soy-free.

Vitamin K2 MK-7 is an effective activator of osteocalcin, the protein essential for directing calcium into the bones and teeth. Beyond bone health, vitamin K2 MK-7 plays a critical role in cardiovascular protection and health. Vitamin K2 activates matrix Gla protein (MGP) in

the blood which inhibits calcification of arteries and other soft tissues. Studies of vitamin K2 MK-7 and cardiovascular health show a significant reduction in arterial stiffness and slower progression of calcification (an independent predictor of cardiovascular disease).

CanPrev's K2 is suspended in a medium chain triglyceride (MCT) oil base*. MCT oil consists of stable fatty acids that enhance the absorption of fat-soluble nutrients like vitamin K2.

K2 Drops

30mcg of Vitamin K2
(menaquinone-7, K2VITAL®)

K2 Softgels

120mcg of Vitamin K2
(menaquinone-7, K2VITAL®)
*organic coconut oil base

Available formats

15ml liquid

120 Softgels

Ideal for



Most adults



Bone & Dental



Cardiovascular



People with
sensitivity to soy



K2VITAL®

By Kappa Bioscience



D3 & K2 Drops & Softgels

CanPrev's D3 & K2 (K2VITAL®) offers a unique form of MK-7 that is derived from the organic synthesis of non-soy plant oils (geraniol and farnesol), yielding a pure, bio-active, stable and 100% trans form that is soy-free.

Vitamin D3 and K2 work synergistically to influence bone mineral strength. Vitamin D3 is a well-known and essential fat-soluble vitamin required for dietary calcium absorption in the intestinal tract. Vitamin K2 MK-7 is an effective activator

of osteocalcin, the protein essential for guiding calcium into bone and teeth matrix. K2 MK-7 also activates MGP, a specialized protein that ensures the calcium traveling in the bloodstream reaches the bone and does not deposit in the arteries.

CanPrev's D3 & K2 fat-soluble vitamins are suspended in a medium chain triglyceride (MCT) oil*. MCT oil consists of stable fatty acids that enhance the absorption of fat-soluble nutrients.

K2 & D3 Drops

250IU of Vitamin D3
(cholecalciferol)

30mcg of Vitamin K2
(menaquinone-7, K2VITAL®)

Available formats

15ml liquid

K2 & D3 Softgels

1000IU of Vitamin D3
(cholecalciferol)

120mcg of Vitamin K2
(menaquinone-7, K2VITAL®)
*organic coconut oil base

120 Softgels

Ideal for



Most adults



Osteoporosis



Cardiovascular



People with
sensitivity to soy

Frequently Asked Questions

How is CanPrev's K2 (K2Vital®) different from other vitamin K2 products?

CanPrev's K2 (K2VITAL®) offers a K2 MK-7 that is produced using an organic synthesis method. Most K2 MK-7 products on the market are derived from a soy fermentation called natto. While both methods produce MK-7 that is identical to that found in nature, organic synthesis offers a few additional benefits.

First, it produces a product made up of 100% "all-trans" isomer MK-7 molecule - the kind that our body can use to activate enzymes. Fermentation processes produces a mixture of cis and trans isomer MK-7, which is not as bioavailable.

Second, CanPrev's MK-7 is sourced from Norwegian and German plant oils rather than soy. This is a good choice for anyone who may have soy sensitivities. It is soy-free.

Third, unlike in fermentation, MK-7 molecules derived by organic synthesis do not need to be extracted and purified - removing the need for solvents in the manufacturing process.

Where do you source your raw materials from?

Our K2 MK-7 is synthesized from plant oils (farnesol and geraniol) that are sourced from Norway and Germany.

Do you add anything else to your K2 MK-7?

Since K2 is a fat-soluble vitamin we've added MCT (medium chain triglyceride) oil derived from palm and/or coconut oil to help improve absorption.

Most K2 products are derived from soy. Can I take your product if I have a soy allergy?

Yes, all of CanPrev's K2 products would be suitable for people who have a sensitivity to soy. CanPrev's Vitamin K2 MK-7 offers a unique form of MK-7 that is non-soy derived, produced through an organic synthesis process. In addition, CanPrev's Vitamin K2 products are also gluten, dairy, and corn free.

Are your K2 products GMO free?

Yes, our line of K2 (K2Vital®) formulations are GMO-free.

Can I get enough K2 from dietary sources?

We encourage you to try and get as much dietary vitamin K2 as you can from your diet first. We recommend including natto into your diet. Natto, an extremely popular fermented soy bean dish from eastern Japan, is one of the best sources of K2 MK-7 you can find in food. Unfortunately, it's somewhat hard to find outside of Japan, as well as being a bit of an acquired taste.

Closer to Canada, K2 in food is a little harder to find. Fermented cheese is an option - one would have to consume around 60 grams of hard cheese daily to reach an effective amount of vitamin K2. Obtaining enough K2 through diet alone is somewhat difficult - supplementation is a good way to ensure you attain recommended levels.

References

Can I supplement with vitamin K2 if I'm currently taking prescription anticoagulants like warfarin?

Blood thinners work by inhibiting the action of vitamin K (particularly K1 needed for clotting). We recommend that you consult with your healthcare practitioner before incorporating vitamin K2 into your daily regime.

**Question not answered?
Let us know.**

info@canprev.ca
t. 888 226 7733



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The background of the image is a vast, high-altitude mountain landscape. In the foreground, a dark, rocky ridge slopes down from the right towards the left, where a large, bright white snowfield or glacier patch is visible. In the distance, a range of jagged, snow-dusted mountain peaks stretches across the horizon under a sky filled with soft, white clouds. Two small figures of people are standing on a distant ridge, providing a sense of scale to the immense landscape.

Good health is the gateway to a good life, whether it's feeling good enough to put in a productive day's work, taking in a spectacular view, keeping up with the pack on a run, playing hide and seek with the kids, or just feeling extraordinary, everyday.

CanPrev exists so that you can live the life you want, however you want, without limitations. We want to provide you the knowledge and tools to help you find your own road to good health, and the road to greater adventures.


Our reason for being

CanPrev grew out of a desire to make natural medicine safe, effective and accessible to everyone. Good health is at the heart of all good passions. It is behind every shout-worthy accomplishment, every mountain climbed, every hard-earned victory.

It involves understanding how your body works. A strong collaboration with practitioners. And supplements you can trust are reliable and powerful. These are the core values of a company started by a partnership between determined patients and natural health practitioners.

We are focused on making the best possible products that informed people and real practitioners can rely on. It demands really understanding root causes. It requires understanding the role of every ingredient before anything goes into a capsule. And it insists on the highest standards of purity and potency.

Staying true to our mission has helped to create a company that we are proud to work for. And for over a decade, our passion for good health has driven us as much as it has sustained us. We're working to put your health back into your hands.

A portrait of Tanya Salituro, a woman with long dark hair, smiling warmly. She is wearing a blue long-sleeved top. The background is a blurred wooden wall.

A cancer survivor and busy mother of four, Tanya Salituro founded CanPrev in 2005 to share the passion she developed for natural health during her three separate journeys with breast cancer.

“Natural health is about the whole person. It goes beyond treating the symptoms - it also strengthens the body, mind and spirit. It leads to stronger people, stronger families, stronger communities and a stronger planet.”

Tanya Salituro
Founder, CanPrev

Why choose us?



In-house experts

Natural health practitioners are involved in everything we do: research & development, quality assurance, and education. They shape how we think and how we act - always in the best interests of the people using our products.



Premium ingredients

Only the finest quality materials are chosen, and our team thoughtfully reviews every ingredient to meet our exact specifications for identity, purity and potency.



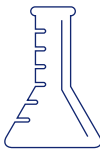
Used by practitioners

Health professionals believe in CanPrev and trust our research, ingredient selection and formulations. Canadian practitioners confidently recommend them in practice.



Quality guaranteed

Health Canada licensed and manufactured at GMP licensed Canadian facilities. Every batch is tested by independent laboratories for that extra level of quality.



Advanced formulations

Our formulations combine the latest research with the best creative and critical thinking.



We are Canadian

CanPrev is proudly Canadian-owned, with natural health products developed by Canadian licensed healthcare practitioners and made right here in Canada.

Courage.

Being responsible for your future health.
It's an act of courage.

It's the act of eating home-cooked, not
fast food. Walking more and driving less.
Seeking answers but not easy answers.

It's paying attention to symptoms.
Understanding your body and making
decisions. Putting yourself to bed when
you're too tired to care. Helping yourself
when no one else can help.

We know that these acts, while
seemingly simple, are not easy. But
they're important, because the best
health care happens when
you care about your own health.

By taking back control of your health,
you inspire us to create the best
possible natural health options we
can, set to the highest standards.
Health products that practitioners
and responsible Canadians can use.

We're driven to help those who help
themselves.



Jamie Junker
Mountain endurance athlete
& CanPrev ambassador
2016 achievements
Elevation gained: 190,357 m
Distance travelled: 2,500 km
Summits reached: 172

Understand your health needs, then take advantage of more than **60 premium natural health products** to achieve your goals. Designed by natural healthcare practitioners to offer therapeutic doses, the best ingredient forms, and evidence-based formulations that make sense.

THERAPEUTICS



Adrenal-Pro™



Blood Sugar Support



Cold-Pro™



Detox-Pro™



Digestion & IBS



Eye-Pro™



Fibre Flow™



Healthy Heart™



Healthy Hormones™



Healthy Lungs™



Immuno Multi™



Joint-Pro™



Joint-Pro™ NEM



Meno-Prev™



Mind-Pro™



Osteo Prolong™



Pain-Pro™



Prostate-Pro™



Slim-Pro™



Thyroid-Pro™

PRO-ESSENTIALS



5-HTP 100



Adult Multi



Alpha Lipoic
Acid 600



Antioxidant Network™



Calcium 200



Chromium 200



Curcumin-Pro™



D3 Softgels



D3 & K2 Softgels



I-3-C 200



Iron
Bis-Glycinate 20



Iron
Bis-Glycinate 25



K2 Softgels



L-Theanine



Magnesium
Bis-Glycinate
200 Gentle



Magnesium
Bis-Glycinate
140 Extra Gentle



Magnesium
Bis-Glycinate
80 Ultra Gentle



Magnesium
Bis-Glycinate 200
Gentle Powder



Magnesium +
GABA & Melatonin
for Sleep



Magnesium +
Taurine, B6 &
Zinc for Cardio



Magnesium
Malate



Omega-Pro™ HP
40/20



pH-Pro™



Prenatal Multi



Pro-Biotik™ 15B



Pro-Biotik™ Powder



Resvera-Pro™



Selenium Glycinate 200



Synergy B™



Synergy C™



Ubiquinol 100



Zinc



CanPrev Core
for Men



CanPrev Core
for Women



ElectroMag™



Magnesium
Bisglycinate 300
Ultra Gentle Liquid



Joint Pro
Concentrate



D3 & K2 Drops



D3 Drops



D3 Drops
for kids

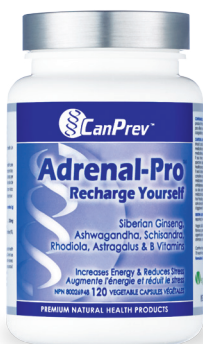


K2 Drops



Oil of Oregano

FEATURED PRODUCTS



Adrenal-Pro™

- Helps increase energy and reduce stress and fatigue
- Enhances physical and mental performance
- Provides an improved sense of well being



Immuno Multi™

- Advanced daily multivitamin and multi-antioxidant
- 21 essential vitamins and minerals
- 10 powerful antioxidants
- The ideal core nutritional platform for all adults



Thyroid-Pro™

- Synergistic blend of nutrients and herbs that helps to support the healthy functioning of the thyroid gland
- Contains iodine naturally sourced from bladderwrack
- Contains the important cofactors selenium, zinc and copper



Cold-Pro™

- For colds, flus, and more
- Supports optimal immune function
- Speeds recovery



Healthy Hormones™

- Relieves menstrual cycle symptoms and PMS
- Relieves pain, breast tenderness and nervous tension
- Includes 400mg of Indole-3-carbinol to detoxify harmful estrogen by-products
- For estrogen dominance related conditions



Meno-Prev™

- For menopausal and perimenopausal complaints
- Relieves hot flashes, night sweats and nervous tension
- Support for mood, memory and libido
- Includes an equivalent of 3000mg maca per daily dose



Prostate-Pro™

- Reduces prostate swelling
- Improves urinary system complaints
- Supports optimal prostate health and libido
- Provides 1500mg of Maca per dose



Blood Sugar Support

- Regulates sugar levels
- Provides antioxidant protection
- Provides support for eyes and nerves

FEATURED PRODUCTS



Pro-Biotik™ 15B

- Helps restore natural gut flora
- Shelf stable with a minimum 15 Billion CFU
- 5 critical, balanced, therapeutic species
- Contains bacteria naturally found in the human GI tract



Synergy B™

- Complete B complex formula in preferred forms like L-5-MTHF and methylcobalamin
- 200mg of L-theanine daily for promoting mental relaxation
- In a base of nutrient-rich spirulina



L-Theanine

- Each vegetable capsule contains a 250mg daily dose of L-theanine
- Promotes a restful, relaxed state without diminishing alertness
- 90 day supply



ElectroMag

- 150mg of elemental magnesium with vitamin C and electrolytes, all in a refreshing effervescent drink.
- Convenient, easy-to-enjoy sachets for making sure you get the magnesium your body craves
- Easy to absorb bisglycinate form



Curcumin-Pro™

- 1200mg daily of pure absorbable curcumin
- 100% curcuminoids from turmeric
- Potent antioxidant and anti-inflammatory action
- Absorption enhanced with phosphatidylcholine and bromelain



Magnesium Bisglycinate 200

- Delivers a potent, therapeutic dose of 200mg of pure elemental magnesium
- A form of magnesium that has superior absorption and is gentle on the bowels
- Easy to swallow vegetable capsule with no fillers.



Magnesium Bisglycinate 300

- 300mg of pure elemental magnesium in every tablespoon
- Magnesium that is easy to absorb and gentle to absorb
- Ideal for those with sensitive stomachs and conditions such as IBS, Crohn's and colitis



Joint-Pro Concentrate

- Complete joint pain relief formula with hydrolyzed collagen
- Combats pain and inflammation
- Liquid form for fast and optimal absorption



Pangnirtung Fjord, Nunavut

The CanPrev Promise

We take your health as seriously as you do, and we want you to feel confident about choosing CanPrev. If you are not 100% satisfied with your CanPrev product, just return it where you bought it for a full refund, or call us for a hassle-free replacement or exchange.

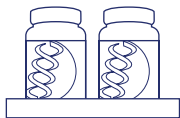
Whatever the reason, whatever the product, we'll do what it takes to make it right. Every time. That's our promise to you.

Find CanPrev



Natural health practitioners

Naturopathic doctors, nutritionists and other healthcare practitioners are all good sources for obtaining great advice and getting you started on the road to good health! **Ask your ND today**



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www.canprev.ca/find

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A comprehensive 148-page guide to CanPrev's natural products, complete with detailed descriptions and practical health advice.

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Magnesium Primer

The ultimate primer on magnesium. Learn why magnesium is important, how it works in your body, strategies to assess how much you need and more.

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Other bone health products

Magnesium Bis-Glycinate 200 **Gentle**
Magnesium Bis-Glycinate 140 **Extra Gentle**
Magnesium Bis-Glycinate 80 **Ultra Gentle**
Effervescent Drink Mix **ElectroMag**

Osteo Prolong
Vitamin D3 Drops and Softgels
Vitamin D3 & K2 Drops and Softgels

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