What’s New With Vitamin K2: New Discoveries on a Critical Nutrient

Susan Allen RDN, CCN
Hosts Kiran Krishnan!
Vitamin K2-7

Defining the structural integrity and rate of aging in virtually every tissue in the body and new discoveries in the function of this critical nutrient.

Kiran Krishnan, Chief Science Officer, Physician’s Exclusive, LLC.
Analogues

- Vitamin K1 (Phylloquinone) can be found in leafy green vegetables, such as spinach, kale, collards, and broccoli. The greener the plant, the higher the vitamin K content.

- Vitamin K2 (Menaquinone), is the form produced by intestinal bacteria and also derived from putrefied fish meal, natto, fermented cheeses.

![Vitamin K1 structure](image1)

![Vitamin K2 structure](image2)
Mechanism

The formation of gla residues within several proteins of the blood clotting cascade is critical for their normal function. The presence of gla residues allows the protein to chelate calcium ions and thereby render an altered conformation and biological activity to the protein.

At this time more than 12 human Gla-Proteins have been discovered.
Well Known Tissues in Need of vitamin K

- clotting factors II, VII, IX, X, C, S, Z
- osteocalcin
- matrix Gla-protein

Vitamin K
Principles for vitamin K uptake in the tissues

- The liver takes what it needs. Vitamin K-dependent coagulation factors are synthesized in liver. Hence, severe liver diseases result in lower blood levels of vitamin k-dependent clotting factors and increased risk of uncontrolled bleeding.

- The remaining K is left for other tissues.

- K-deficiency mainly occurs in extra-hepatic tissues.

- Effects of K-deficiency will be most pronounced in bone, cartilage and arteries.
VITAMIN K AND BONE HEALTH

Healthy bone  Osteoporotic bone
The Role of K2 in Building Bone and Preventing Bone Loss

Vitamin D (inactive form) → Vitamin D3 (active form) → Stimulation by D3 → Osteoblast cells – bone building cells → Release of osteocalcin

Glu-osteocalcin (inactive form) → Gla-osteocalcin (active form) → Calcium → Adding calcium and building bone → Calcium breakdown of bone

Vitamin K2-7

X
VITAMIN K2 AND OSTEOCALCIN

- Osteocalcin is a vitamin K-dependent protein that creates the bone matrix upon which calcium crystallizes

- Osteocalcin - provides the “glue” that holds calcium in the bone – giving structure and order to bone tissue; without it bone would be fragile and easily broken

- Vitamin K “activates” osteocalcin through a process called “carboxylation”

- Without carboxylated osteocalcin, calcium cannot be properly utilized for bone structure
• Szulc et al: ucOC inversely correlates with BMD

• Knapen et al: ucOC inversely correlated with BMD

• Vergnaud et al: serum ucOC predicts hip fracture

• Luukinen et al: serum ucOC predicts hip fracture

• Szulc et al: high ucOC // 6-fold increased fracture risk
Natural Vitamin K2 as Mk-7 from Natto is Effective

• 2001 -- Kaneki – high consumption of MK-7 levels from natto resulted in better levels of activated osteocalcin and a reduced risk fracture

• 2006 -- Ikeda - natto consumption helps prevent the development of osteoporosis

• 2008 – Yaegashi showed that better vitamin K status attributed to Natto resulted in the reduction of hip fracture risk.

Booth, J Clin Endocrinol Metab 2008
HIP FRACTURE INCIDENCE AND K2 AS MK-7 2008

• Dietary intakes of calcium, magnesium, vitamin D, and vitamin K were analyzed in nationwide survey (Japan)

• Hip Fracture Incidence was much higher in the West

• The strongest inverse correlations were found for vitamin K in both men and women

• Calcium intake had weak or null associations between the standardized incidence ratio

• Mk-7 from Natto – attributed to the reduced risk in Eastern Populations

Yaegashi Eur J Epidemiol 3-2008
VITAMIN K₂ AND VASCULAR HEALTH
First it was blood cholesterol that could give you an early warning that a heart attack might be around the corner. Then came c-reactive protein. And now that doctors can get a better look at what's inside your heart arteries, they are taking a new interest in something they have always known was present in problem vessels: calcium. Hospitals, clinics and even gyms are touting quick and easy scans that can measure the amount of calcium in your coronary arteries in minutes.

Calcium can then build up in the vessels and stiffen them, laying the foundation for heart disease. Getting one's calcium score is simple, either by electron beam computed tomography (EBCT) or by multidetector CT. Studies show that in every age group people with higher vascular calcium levels have a greater risk of heart attack than do people of the same age with lower scores.
K-vitamins in healthy and atherosclerotic human aorta’s (means from 3 donors)
VITAMIN K₂ AND VASCULAR HEALTH

A high menaquinone reduces the incidence of coronary heart disease in women

Methods and Results: We used data from the Prospect–EPIC cohort consisting of 16,057 women, enrolled between 1993 and 1997 and aged 49–70 years, who were free of cardiovascular diseases at baseline. Intake of vitamin K and other nutrients was estimated with a food frequency questionnaire. Multivariate Cox proportional hazards models were used to analyse the data.

Conclusions: A high intake of menoquinones, especially MK-7, MK-8 and MK-9, could protect against CHD. However, more research is necessary to define optimal intake levels of vitamin K intake for the prevention of CHD.

High dietary menaquinone intake is associated with reduced coronary calcification


Methods: We investigated the association of intake of phylloquinone and menaquinone, including its subtypes (MK4–MK10), with coronary calcification in a cross-sectional study among 564 post-menopausal women. Phylloquinone and menaquinone intake was estimated using a food-frequency questionnaire.

Conclusion: This study shows that high dietary menaquinone intake, but probably not phylloquinone, is associated with reduced coronary calcification. Adequate menaquinone intakes could therefore be...
VITAMIN K INTAKE AND CARDIOVASCULAR DISEASE: THE ROTTERDAM STUDY

• **Objective:** to study the association of dietary intake of K$_1$ and K$_2$ with aortic calcification, CVD, and total death

• **Design:** cross-sectional analysis in healthy adults

• **Setting:** 4807 men and women aged 55 and older; 10 years follow-up

• **Measurements:**  
  - calcification
  - end point (death)
Conclusions:

When consuming daily 45 µg dietary K2 you have:

50% reduction of arterial calcification

50% reduction of cardiovascular death

25% reduction of all cause mortality

as compared to low intake of dietary K2!

There was no correlation for vitamin K1 in this study!

Geleijnse et al. Journal of Nutrition 2004
• Vitamin K2 shown to reduce diabetes risk by 20% in a Dutch population study over 10 years – 38,000 patients

• Vitamin K2 shown to decrease cancer risk. Study on 23,000 German adults. Showed higher K2 intake associated with a lower likelihood of developing and dying of cancer.

• Vitamin K2 shown to reduce prostate cancer risk by 35% in a epic study in 11,319 men taking part in the Heidelberg cohort.
NEW DISCOVERIES IN VITAMIN K2 FUNCTION

A SEEMINGLY OMNIPRESENT VITAMIN.....
Using a technique of Reverse Pharmacology, we made the following discoveries....
NEW DISCOVERIES

- Function in Muscle Contraction
- Function in Nerve Health
- Function in Mitochondria
- Redox Function of Vitamin K2
- Function in Cardiac Function and Output
MITOCHONDRIA FUNCTION

YET ANOTHER MECHANISM

– 1950’s
Redox cycle activity of vitamin K was proposed by Martius, et al.

– 1960’s
At a later date Johnson et al, refuted this claim.
Vitamin K-Mitochondrial Respiration
Mitochondrial Bioenergetics

Mitochondrial Respiration: Test sequence in sea horse XF-96 platform

SupplySideWest 2015 | Dr. Ted Reid, Ph.D
Vitamin K Bioenergetics

Cellular Experiments

Neuroblastoma cell line

Mitochondrial Respiration: Test sequence in sea horse XF-96 platform
Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency.


Author information

Abstract

Human UBIAD1 localizes to mitochondria and converts vitamin K(1) to vitamin K(2). Vitamin K(2) is best known as a cofactor in blood coagulation, but in bacteria it is a membrane-bound electron carrier. Whether vitamin K(2) exerts a similar carrier function in eukaryotic cells is unknown. We identified Drosophila UBIAD1/Heix as a modifier of pink1, a gene mutated in Parkinson’s disease that affects mitochondrial function. We found that vitamin K(2) was necessary and sufficient to transfer electrons in Drosophila mitochondria. Heix mutants showed severe mitochondrial defects that were rescued by vitamin K(2), and, similar to ubiquinone, vitamin K(2) transferred electrons in Drosophila mitochondria, resulting in more efficient adenosine triphosphate (ATP) production. Thus, mitochondrial dysfunction was rescued by vitamin K(2) that serves as a mitochondrial electron carrier, helping to maintain normal ATP production.

“Neuroscientist Patrik Verstreken, associated with VIB and KU Leuven, succeeded in undoing the effect of one of the genetic defects that leads to Parkinson's using vitamin K2. His discovery gives hope to Parkinson's patients.”
Mitochondrial data gave us a clue that perhaps vitamin K2 could regenerate dysfunctional mitochondria in tissue – a great example would be neurodegenerative diseases.

N=30
Dosing: 100mcg/day
Duration: 8 weeks
Results: Well tolerated and significant alleviation of neuropathy

**The effect of vitamin K2-7 in peripheral neuropathy due to Vitamin B12 deficiency and/or diabetes mellitus:**

A Preliminary Study

Kulkarni VK*, Upade DP*, Dound YA**, Jadhav SS*, Bhave AA***, Mehta DS*, Vaidya AB‡

**ABSTRACT:**

Objective: To evaluate the activity and tolerability of Vitamin K2-7 (MK-7) in a series of patients with peripheral neuropathy due to B12 deficiency and/or diabetes mellitus.

Material and Methods: An open labeled clinical study was conducted in 30 patients presenting with peripheral neuropathy and suffering from either megaloblastic anemia (B12 deficiency) and/or diabetes mellitus. Vitamin B12 levels in blood were estimated at baseline and during therapy. Vitamin K2-7 capsules (100 mcg/capsule, twice a day) was given orally for 8 weeks. Patients kept a regular record of the intensity of the symptoms during the baseline and throughout the study. Symptoms included tingling and numbness along with weakness, fatigue and cramps. The intensity of the symptoms was assessed on a Visual Analog Scale (VAS). They were followed up to 8 weeks. Blood biochemical and organ function tests were studied at the baseline, at the fourth week and at the end of the eighth week. Protocol for the study Ethics Committee Approval was obtained from the Ethics Committee of T.N. M.C. & B.Y. L. Nair Ch. Hospital. The trial was registered with Clinical Trial Registry of India (CTR). (CTRI201208002930). Informed written consent was obtained from the patients before enrollment.

Results: Depending on the basal VAS score, the patients were divided in to a moderate group and a severe group. The moderate group had VAS score of 6-8 and the severe group had a VAS score of 8-9. By the end of eighth week, the VAS score in both the groups was reduced to 1-2. The intensity specifically of tingling and numbness has reduced to a much greater extent. It was of interest to observe that ten out of 23 patients of Vitamin B12 deficiency had residual neuropathy symptoms inspite of adequate levels of Vitamin B12 following vitamin B12 administration. The residual neuropathic symptom score reduced following Vitamin K2-7 therapy. Vitamin K2-7 was well tolerated clinically and found to be safe as per the organ functions in all the patients. No adverse events were reported during the period of therapy.

Conclusions: This preliminary study has shown that vitamin K2-7 at a dose of 100 mcg twice daily for 8 weeks was well tolerated and safe with a therapeutic activity for the symptoms of peripheral neuropathy. However, the therapeutic efficacy needs to be evaluated further in a larger sample size, with a placebo controlled randomized double blind trial.

KEY WORDS: Vitamin K2-7, diabetes mellitus, megaloblastic anemia, peripheral neuropathy, reverse pharmacology.
Consumption of a MyoMax® (Vitamin K2 Containing Supplement) for 8-weeks was Associated with Increased Maximal Cardiac Output during Exercise

McFarlin BK1,2, Henning AL1,2, and Venable AS1,2

1Applied Physiology Laboratory; University of North Texas, Denton, TX

Cardiac Output – the amount of blood the heart pumps through the circulatory system in one minute

- 23% increase at max HR
- 13% increase at resting HR
- 900+ liter more blood/24hrs
ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

The Mitochondrial Free Radical Theory of Aging (MFRTA) proposes that mitochondrial free radicals, produced as by-products during normal metabolism, cause oxidative damage. According to MFRTA, the accumulation of this oxidative damage is the main driving force in the aging process.

Especially Cardiac Mitochondrial Oxidant Production!

“In a revealing study, a team of researchers showed that muscle tissue of a 90-year-old man contained 95% damaged mitochondria compared to almost no damage in that of a 5-year-old.”

ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

“studies indicated a decrease of cardiac output with aging at rest and with exercise.”

Melvin D. Cheitlin, MD. Am J Geriatr Cardiol. 2003;12(1)

“A substantially reduced output was a consistent finding in older subjects.”

MARTIN BRANDFONBRENER, M.D., MILTON LAN DOW-NE, M.D. AND NATHAN W. SHOCK, PH.D.
CIRCULATION . October 1, 1955
You Are As Old As Your Arteries Are!

Prognostic value of coronary artery calcium screening in subjects with and without diabetes

Raggi, et al. Journal of the American College of Cardiology 2004
ARGUABLY THE MOST IMPORTANT ANTIAGING NUTRIENT

Biological aging is a factor of Mitochondrial Health, Cardiac Output and Vascular Health. It is easy to see that all 3 factors are intertwined and vitamin K2 plays a significant role in improving the health of each of these systems.

- Better perfusion
- Removing Calcium from arteries
- Slowing down the progression of diabetes
- Every cell in the body gets more nutrients and blood supply
- Increases mitochondria function, so each cell can produce more energy and we can regenerate dying cells.
- Prevents aging related tissue degeneration

Nature’s Fountain of Youth!

Dose required is 100-300mcg and is has a linear dose dependent curve.
WHAT CAN VITAMIN K2-7 DO FOR YOU?

- Heart Disease
- Osteoporosis
- Diabetes
- Cancer
- Dementia
- Joint Health
- Facial/Cranial Development
- Skin Health
- Dental Health
- Muscle Function
- Neuropathy – Neurodegenerative diseases
- Mitochondria Restoration
- Cardiac Function
- Aging

And we are all sub-clinically deficient in this key nutrient!!

- Cranenburg ECM, Schurgers LJ, Vermeer C. Vitamin K, the coagulation vitamin that became omnipotent. Thromb Haeomost 2007, 98(1):120-25
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