Vitamin K2-7

Vitamin K2 and the role it plays in reducing multiple chronic diseases

Presented by Kiran Krishnan, Chief Science Officer of Microbiome Labs
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.
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

Vitamin K

- clotting factors II, VII, IX, X, C, S, Z
- osteocalcin
- matrix Gla-protein
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 results 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
The Role of K2 in Building Bone and Preventing Bone Loss

Vitamin D (inactive form) → Stimulation by D3 → Osteoblast cells – bone building cells

Calcium → Adding calcium and building bone

Vitamin K2-7

Gla-osteocalcin (active form) → Release of osteocalcin

Glu-osteocalcin

Calcium → Breakdown of bone

Vitamin K2-7
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
OSTEOCALCIN CARBOXYLATION, BMD AND FRACTURE RATE

• 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
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)
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

Joline W.J. Beulens a,*, Michiel L. Bots a, Femke Atsma a, Marie-Louise E.L. Bartelink a, Matthias Prokop b, Johanna M. Geleijnse c, Jacqueline C.M. Witteman a, Diederick E. Grobbee a, Yvonne T. van der Schouw a

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 important to prevent cardiovascular disease.
**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
ADDITIONAL CLINICALLY PROVEN INDICATIONS

• 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…..
Unitary Hypothesis

“Perfusion, Hypoxia, Energy Balance & Microcirculation Improves significantly with K2”

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.

REDOX CYCLE

\[
\text{NADH} \rightarrow \text{NAD}^+ \rightarrow \Delta \text{ATP} \rightarrow \Delta \text{VO}_2\text{max} \rightarrow \text{ADP} \rightarrow \text{ATP} \rightarrow \text{KH}_2
\]
Vitamin K-Mitochondrial Respiration
Mitochondrial Bioenergetics

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

Cellular Experiments

Neuroblastoma cell line

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

SupplySideWest 2015 | Dr. Ted Reid, Ph.D.
Vitamin K2 is a mitochondrial electron carrier that rescues pink1 deficiency.


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.”

www.sciencedaily.com/releases/2012/05/120511101240.htm
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
Consumption of a MegaQuinone® (Vitamin K2 Containing Supplement) for 8-weeks was Associated with Increased Maximal Cardiac Output during Exercise

McFarlin BK\textsuperscript{1,2}, Henning AL\textsuperscript{1,2}, and Venable AS\textsuperscript{1,2}

\textsuperscript{1}Applied 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+ liters 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.”

By Kirk Stokel

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
WHERE CAN I PURCHASE MEGAQUINONE?

Practitioner Only account www.megasporebiotic.co.uk

Also available from Natural Dispensary

Questions: Arnie@tmcventures.com

TMC Ventures Europe is the exclusive UK & European Distributor for MegaQuinone™ and MegaSporeBiotic™

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