

MenaQ7[®]
Natural Vitamin K2

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Vitamin K

NattoPharma[®]

History

- Discovered in **1929**
- **K** stands for “koagulation”
- **Fat-soluble vitamins** (A, D, E and K)
- New functions are now documented



Henrik Dam



Edward Adelbert
Doisy

Dam and Doisy shared the
1943 Nobel Prize in Physiology
or Medicine for their work on Vitamin K

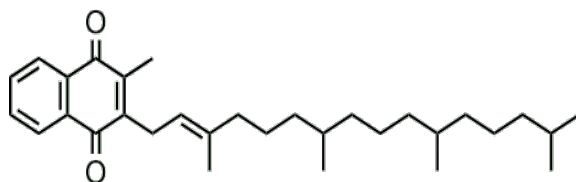


Forms of vitamin K

K family

K1 phylloquinone

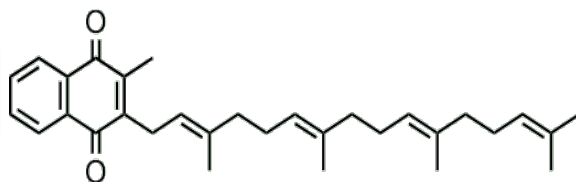
K1



Short half-life
Major tissue to utilize is the liver

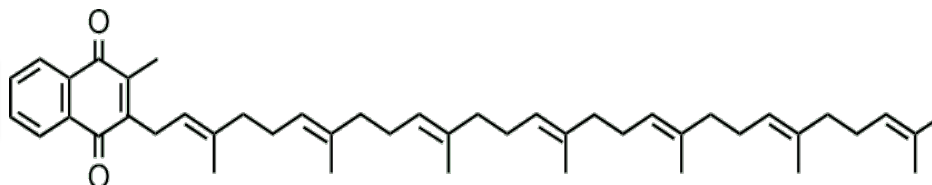
K2 menaquinones

MK-4



Short half-life

MK-7



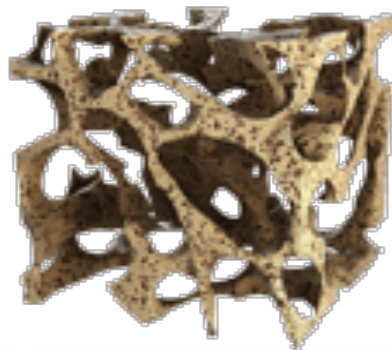
Long half-life, reaches peripheral tissues

Mechanism of Action

Osteocalcin

**Calcium
brought to
the bones...**

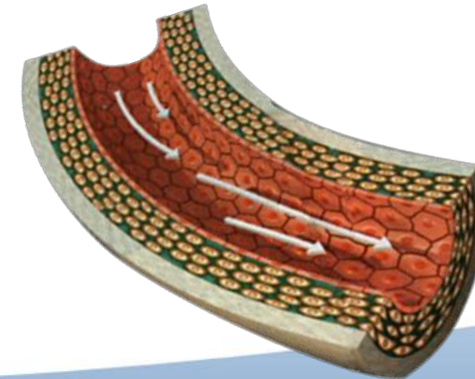
BONE



Matrix Gla Protein (MGP)

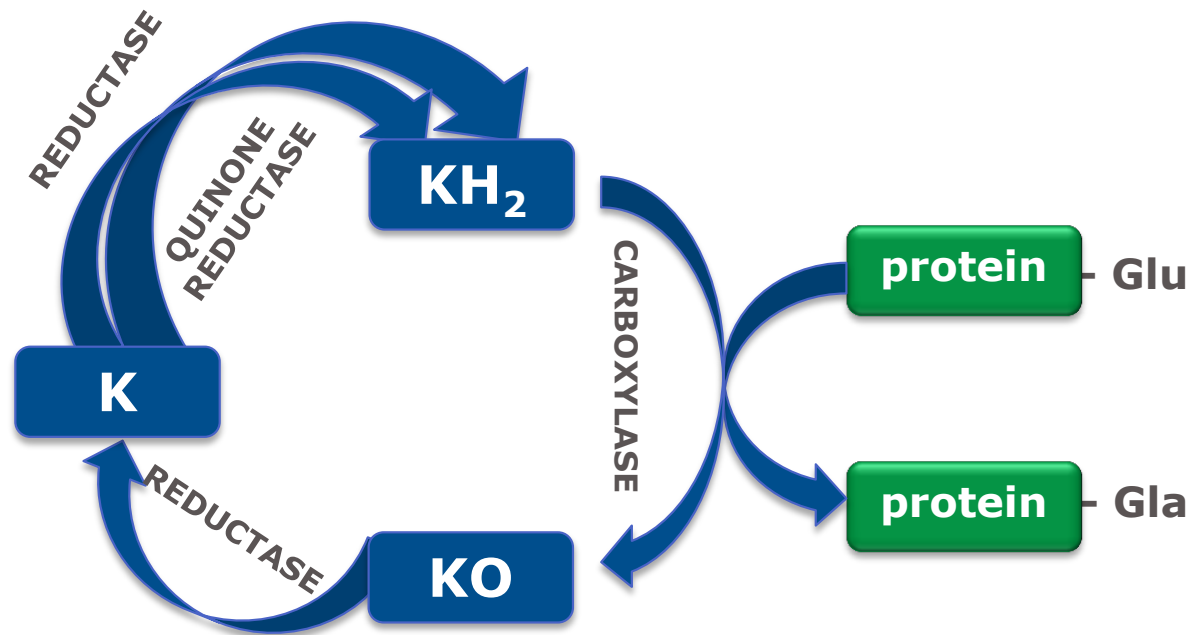
**... and
out of the
Vasculature**

ARTERIES



Function of vitamin K

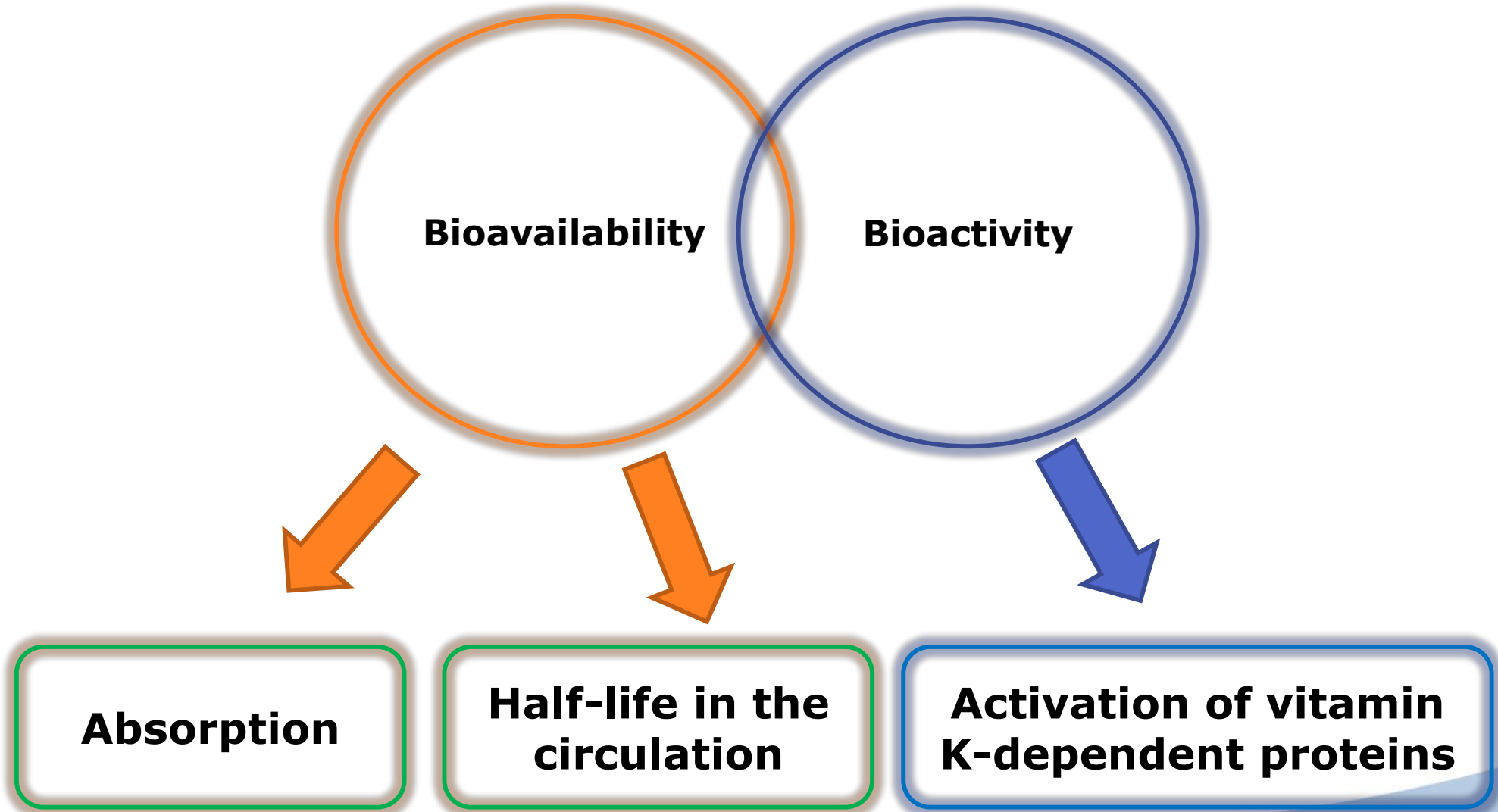
Some proteins need vitamin K to become biologically active



KH₂- vitamin K hydroxyquinone
KO- vitamin K epoxide
K- vitamin

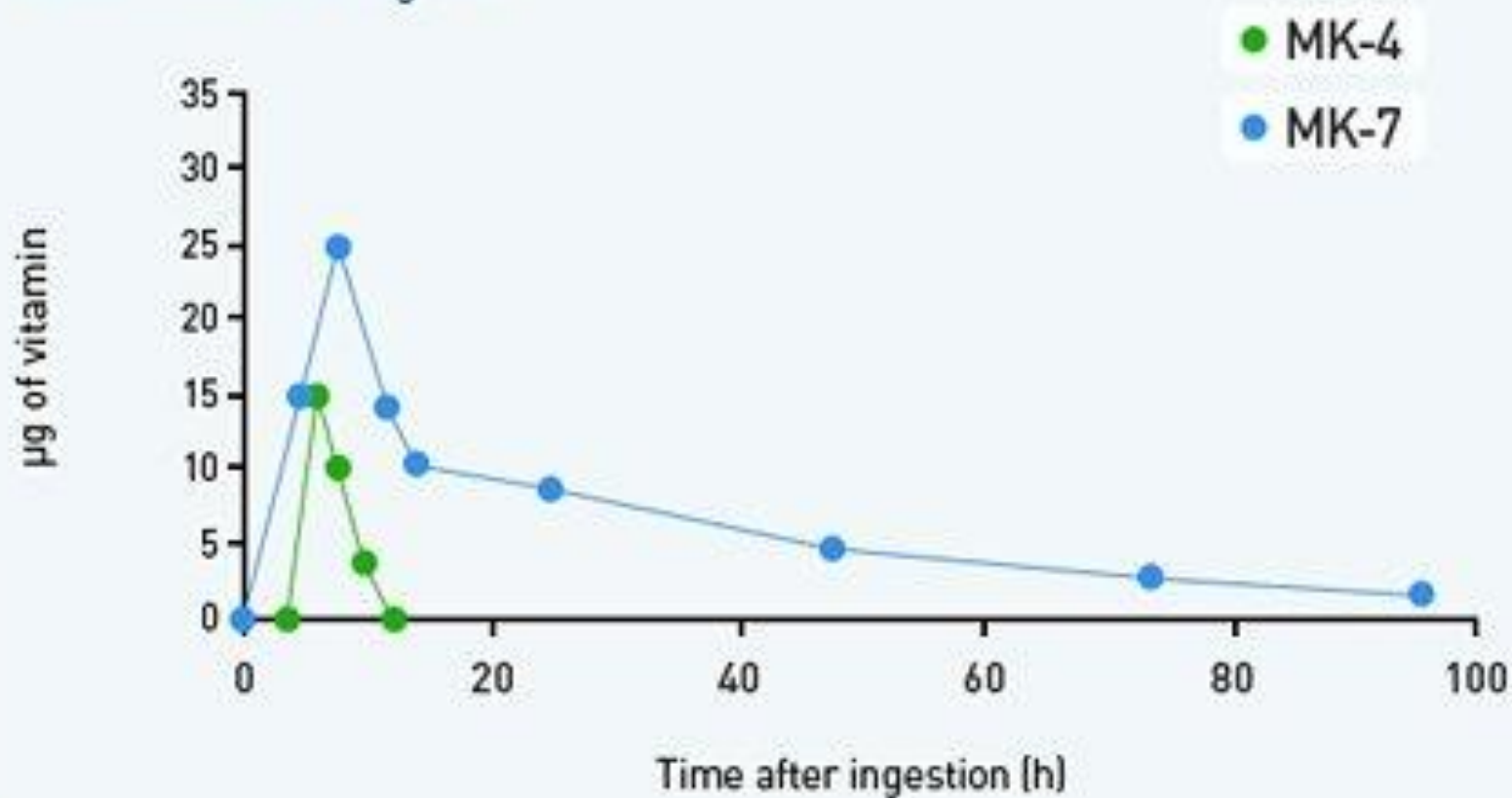
Glu - glutamic acid
Gla - gamma-carboxyglutamic acid

Bio-availability and bioactivity

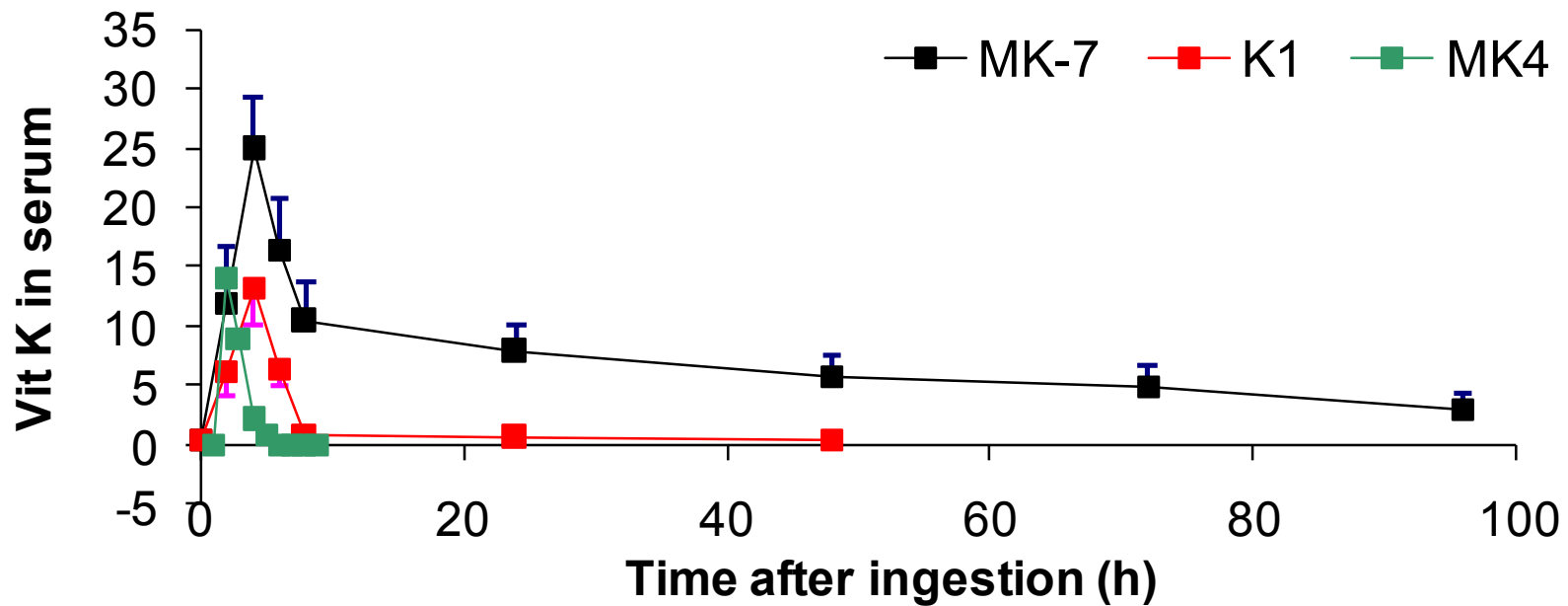


Vitamin K in serum (half life)

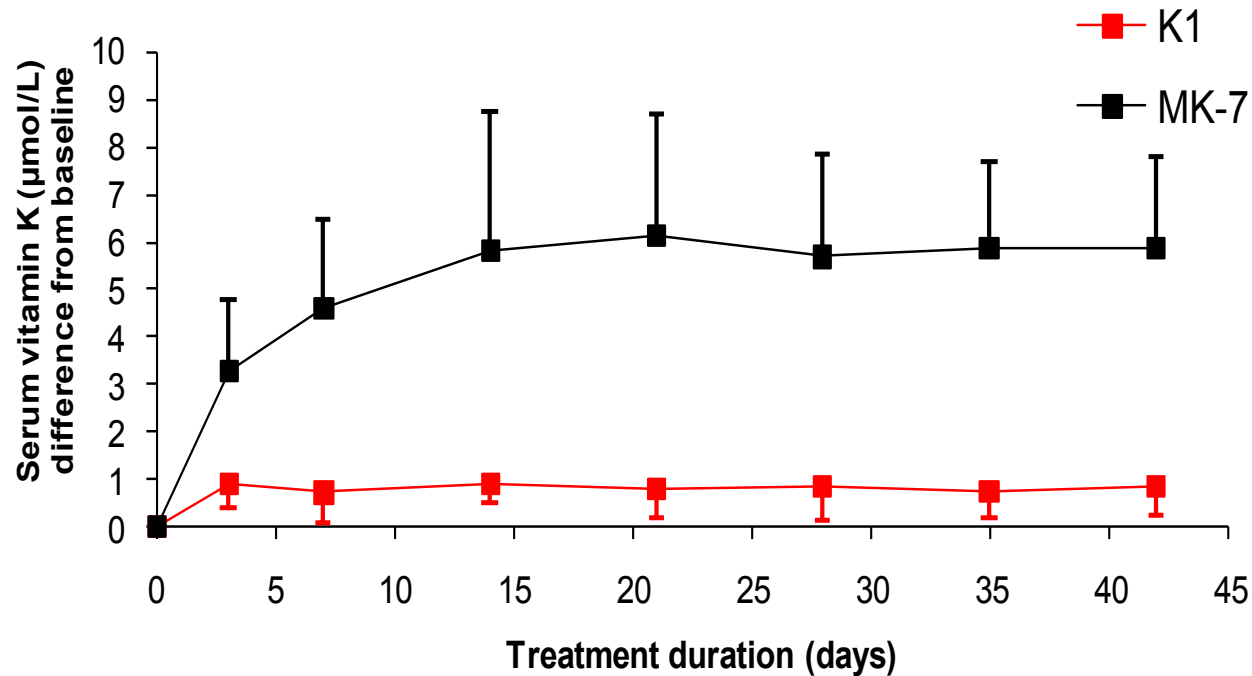
Vitamin K in serum (ng/ml)



MK-7 has superior bioavailability

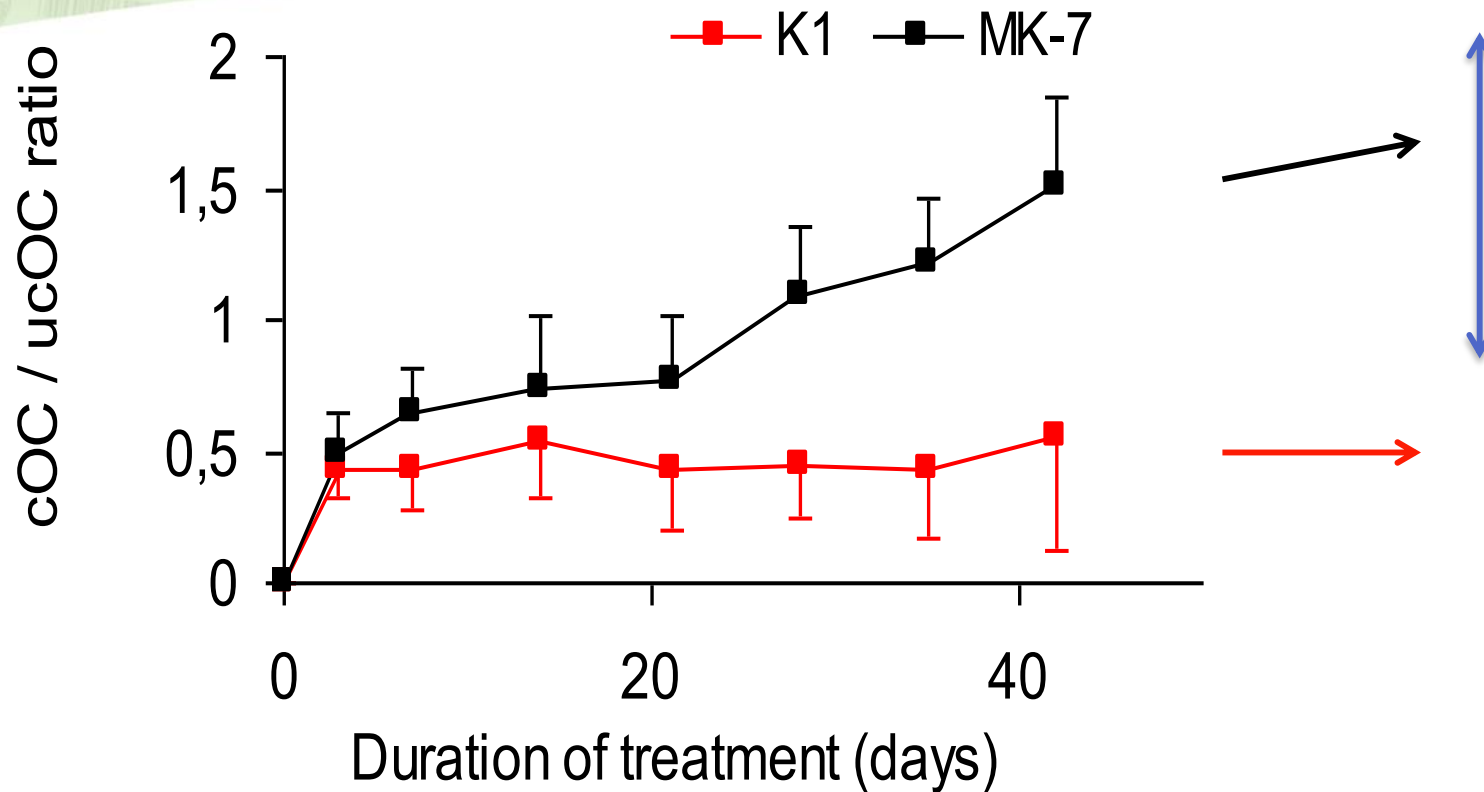


Accumulation during prolonged intake



- No accumulation of K₁ but significant accumulation of MK7
- After 14 days a steady level for MK-7 was reached
- Final level for MK-7 was 7-8 fold higher than for K₁

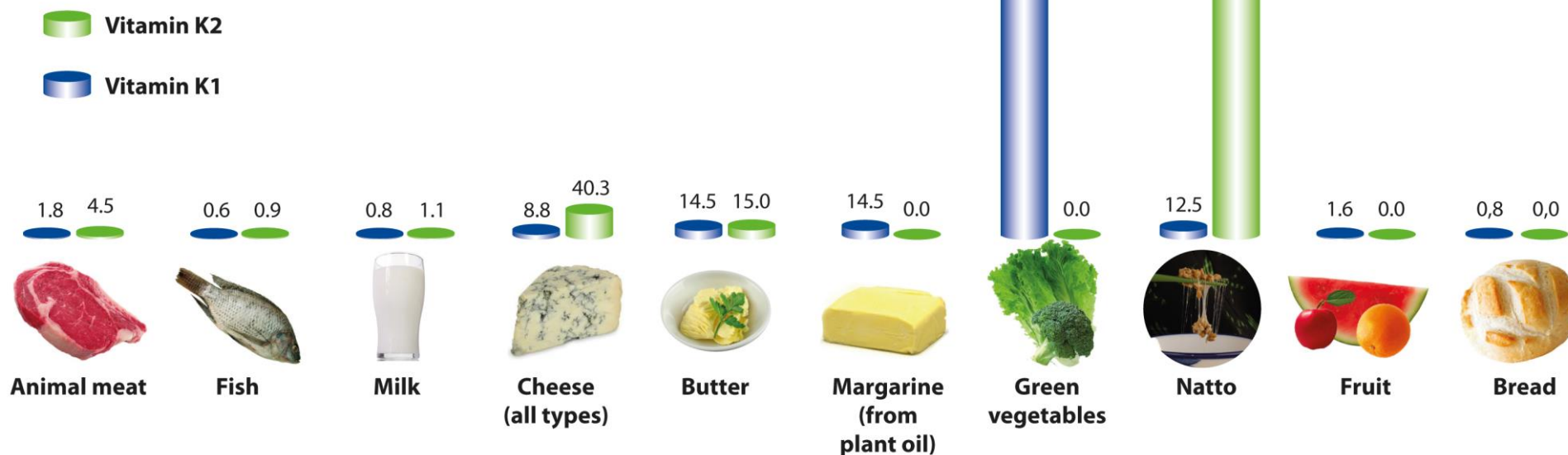
If taken on a daily basis, 45 µg/day of MK-7 is more effective than 240 µg/day of K₁ (twice the RDA!)



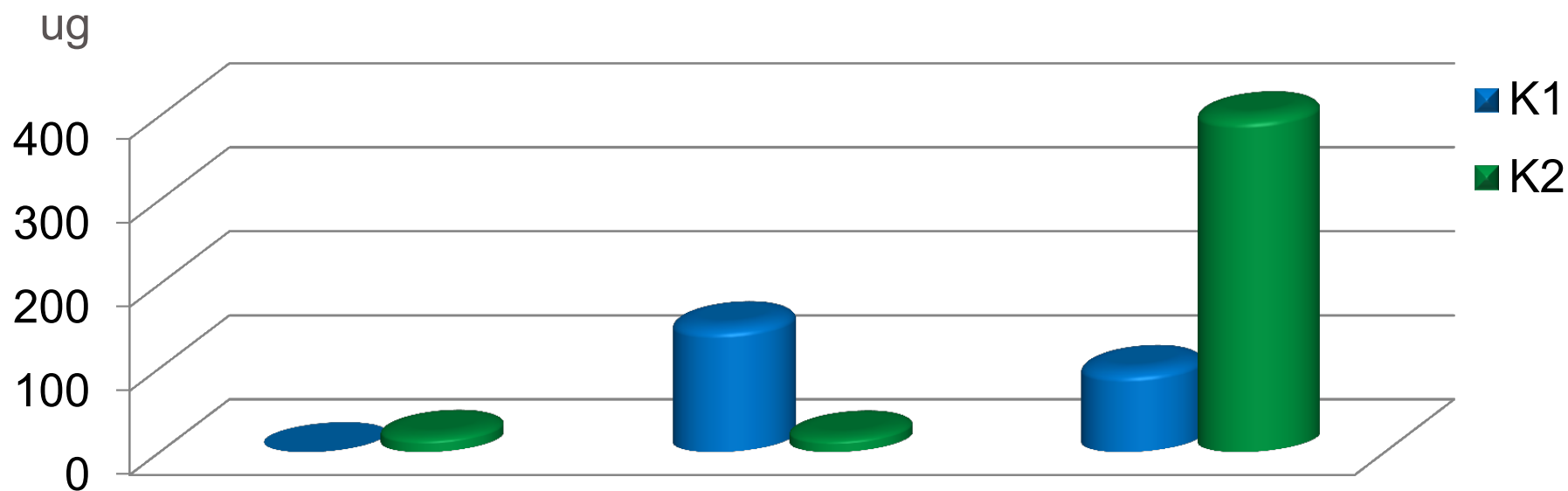
- MK-7 is more effective than K₁ in improving vitamin K status → effect visible after 2-3 weeks
- Effect most pronounced after 6 week
- At that time **MK-7 was over 3 times more effective than K₁**

Dietary sources of vitamin K

Typical amount of Vitamin K1 and K2 in various foods (in µg/100 g food).



Deficiency of vitamin K



Junk food



Western healthy diet



Japanese diet



K1 is the major form of nutritional vitamin K in Europe

Deficiency of vitamin K

Acute disease:

Bleeding

- Haemorrhagic disease of the newborn
- Cerebral haemorrhage
- Wounding

Chronic diseases

- Osteoporosis
- Cardiovascular disease
- Cancer
- Diabetes
- Dementia
- Renal disease
- Osteoarthritis

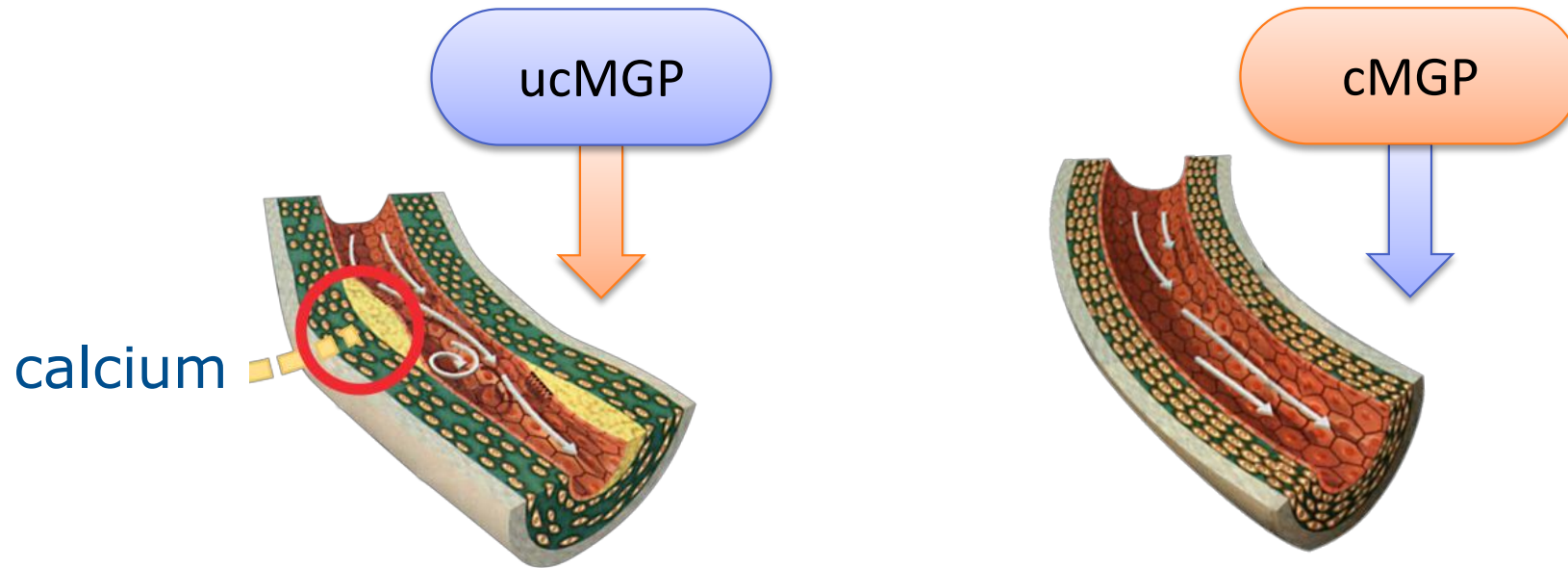
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Cardiovascular Health

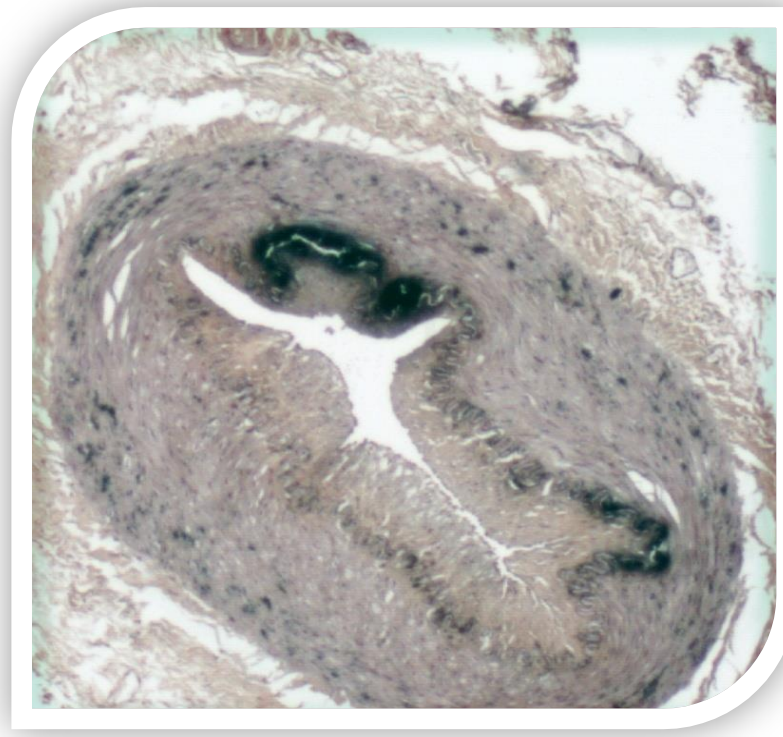
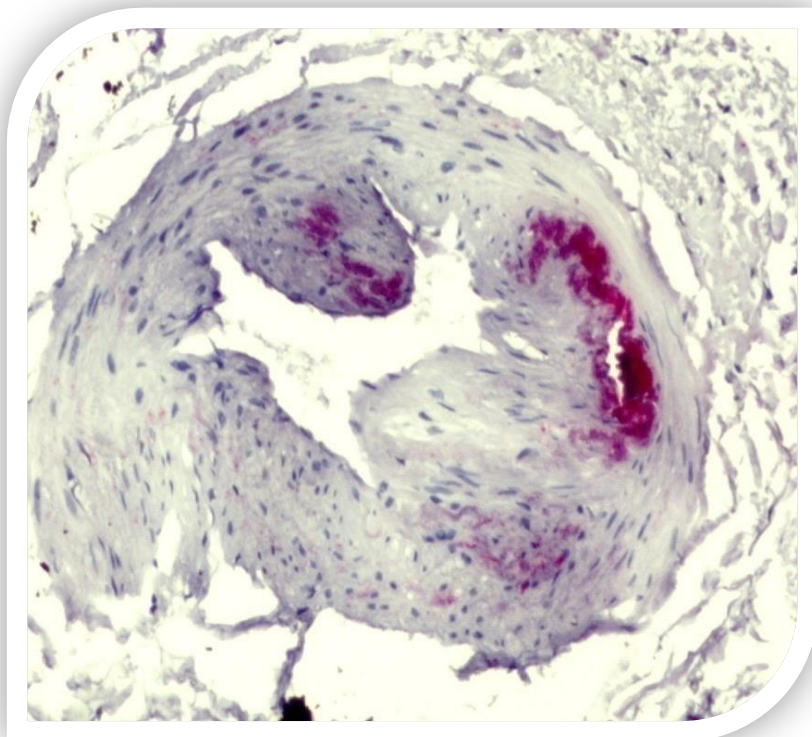
NattoPharma[®]

Calcification process



- Vitamin K deficiency results in undercarboxylation of MGP (ucMGP) that impairs its biological function
- A massive accumulation of ucMGP is present in atherosclerotic plaques
- Recently ucMGP was shown a biomarker for CVD

Inactive MGP "leads" to calcification



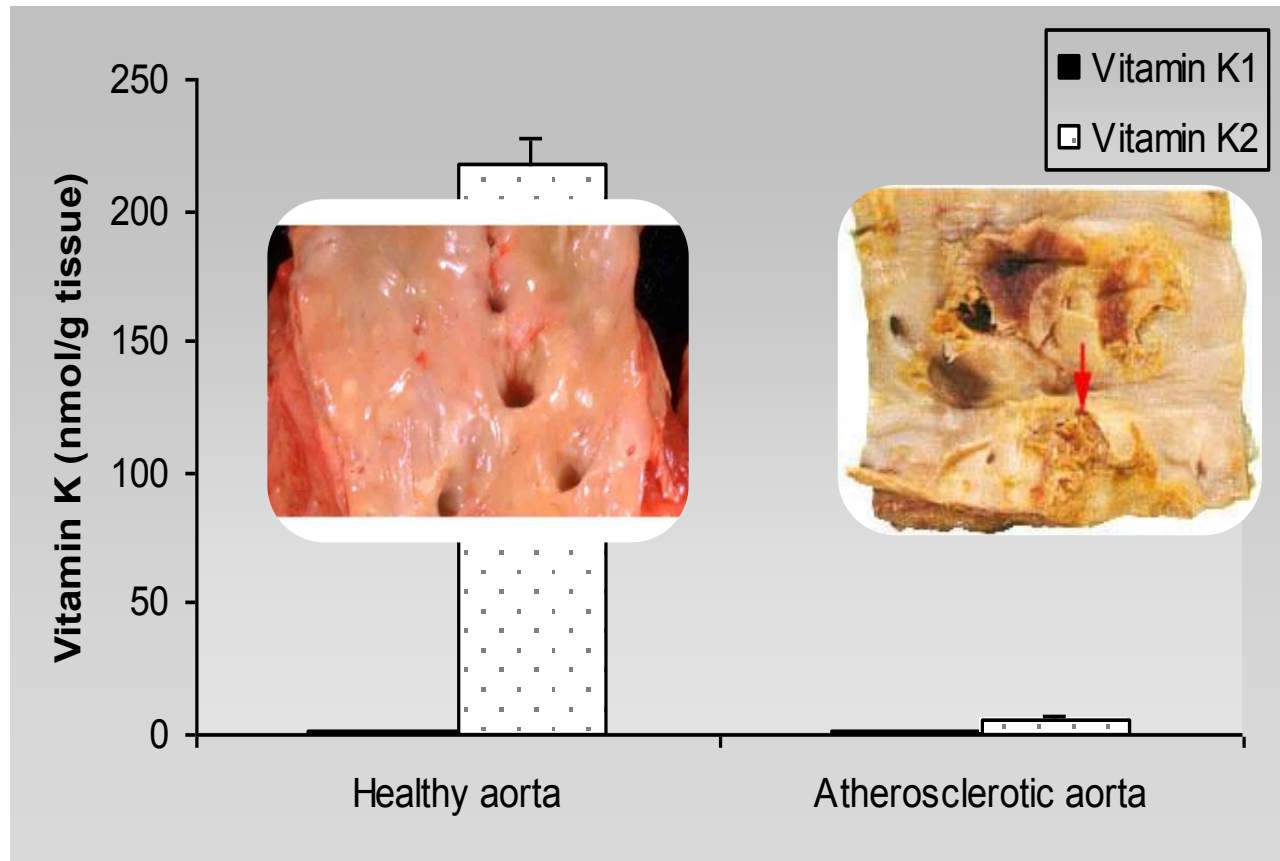
Immunohistochemistry staining

In red: localization
of the inactive MGP

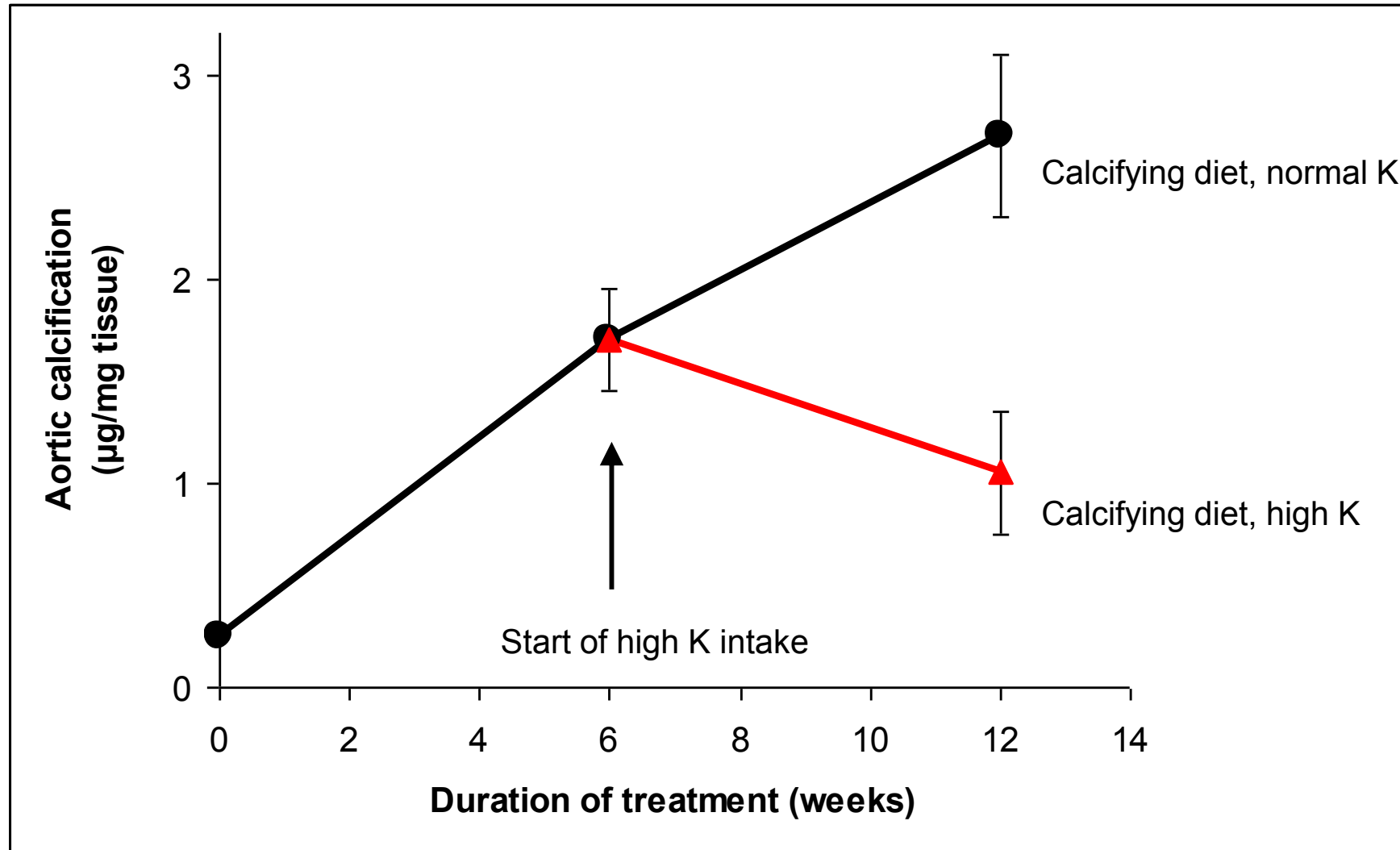
Von Kossa staining.
In black: calcification

Clinical results of vitamin K2 deficiency

K vitamins in healthy and atherosclerotic human aorta:
Biopsies from University Hospital Maastricht

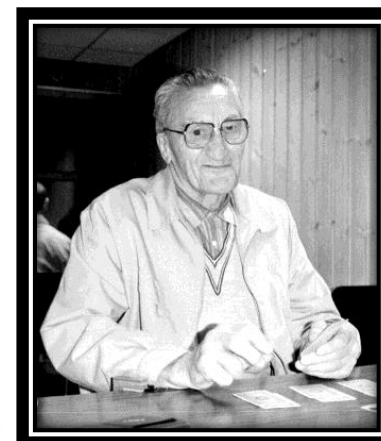
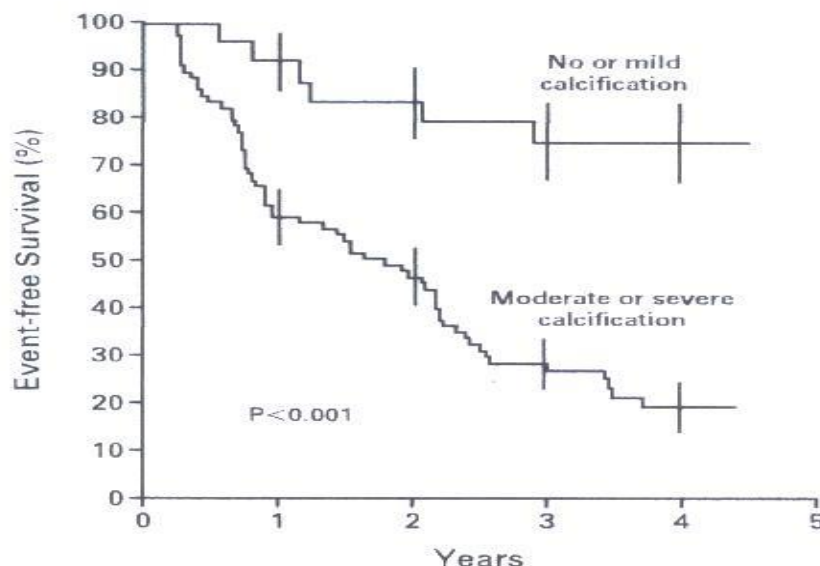
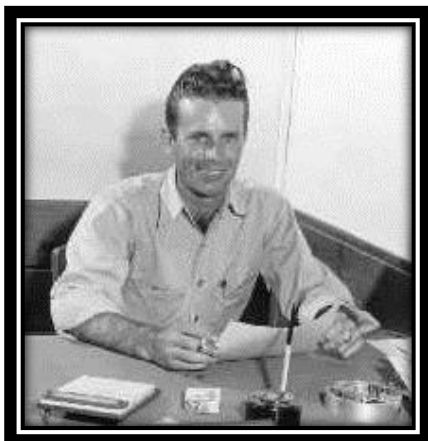


Regression of arterial calcification by vitamin K in rats



Calcification of arteries

Rosenhek, et al. *New England Journal of Medicine* 2000



Age < 40 years; calcification > 1000 units: Biological age 70 years!

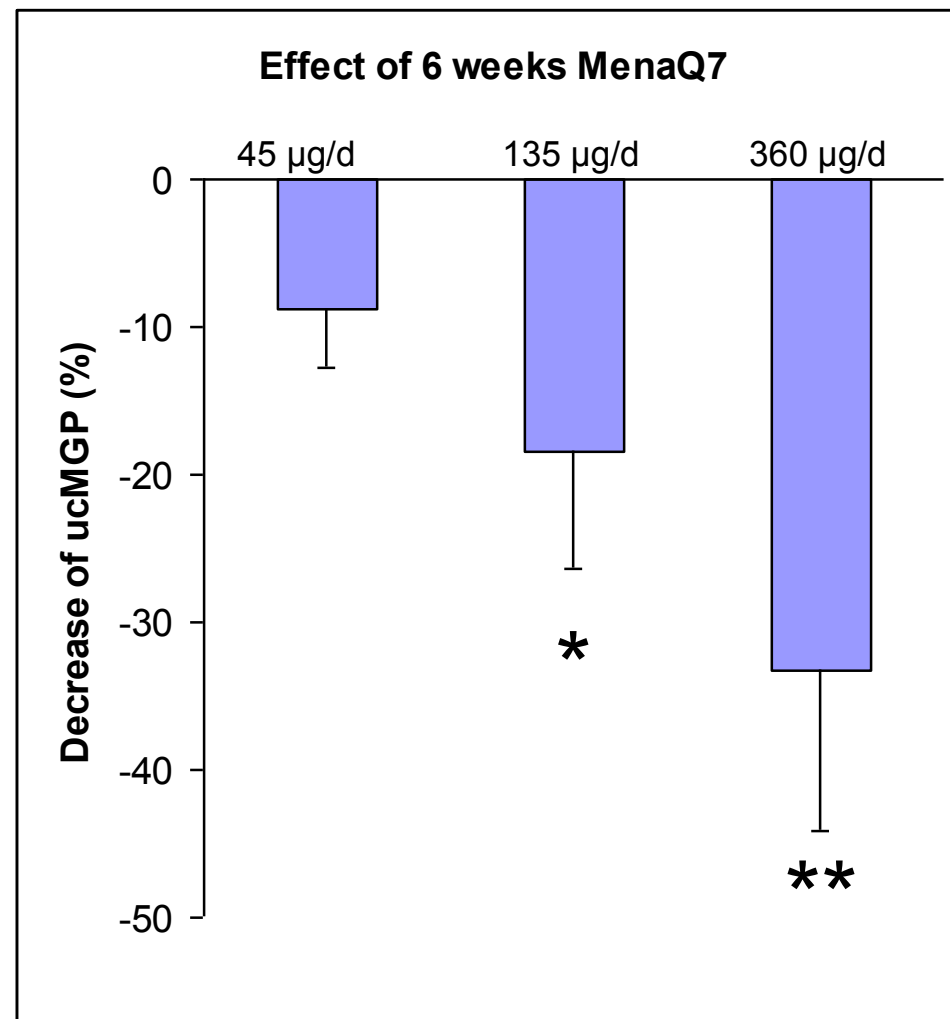
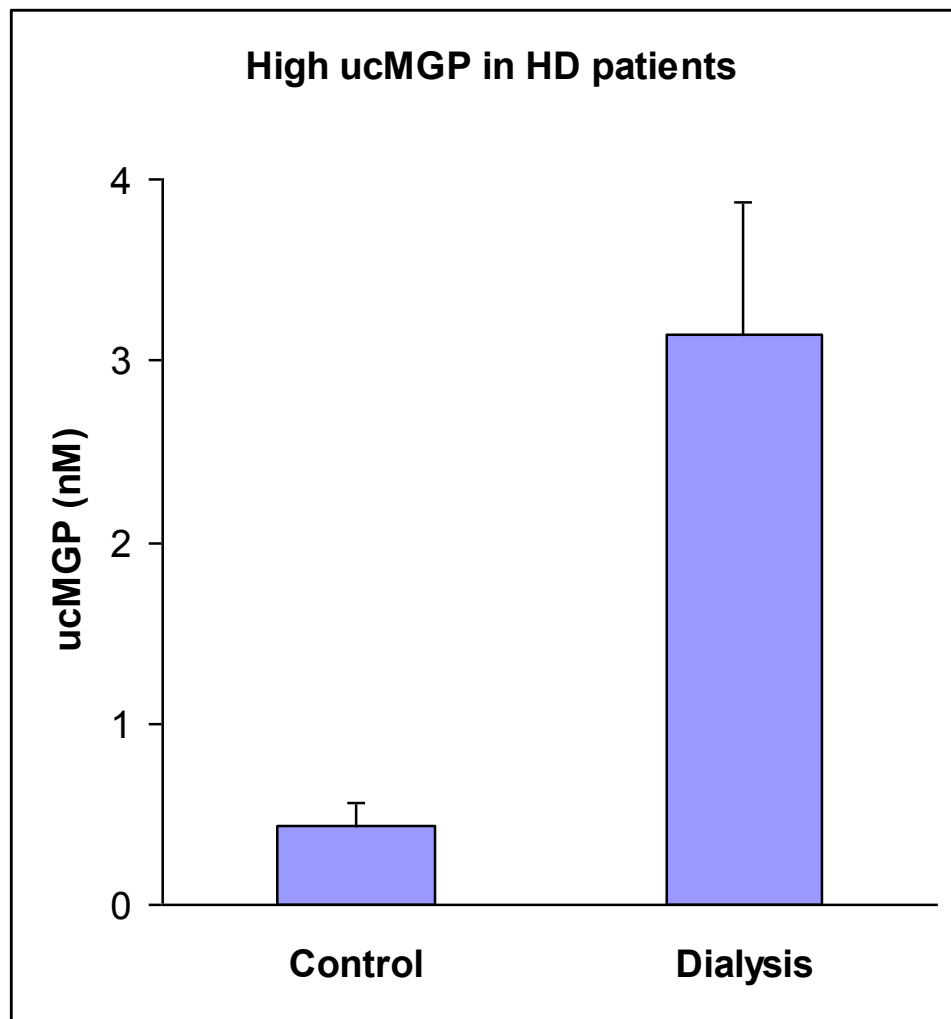
Scores > 400 added up to 30 years to younger subjects

Calcium score < 10: Reduction in observed age by 10 years in subjects older than 70 years

Ref: Shaw et al. *Atherosclerosis* vol 188, p. 112 ; 2006

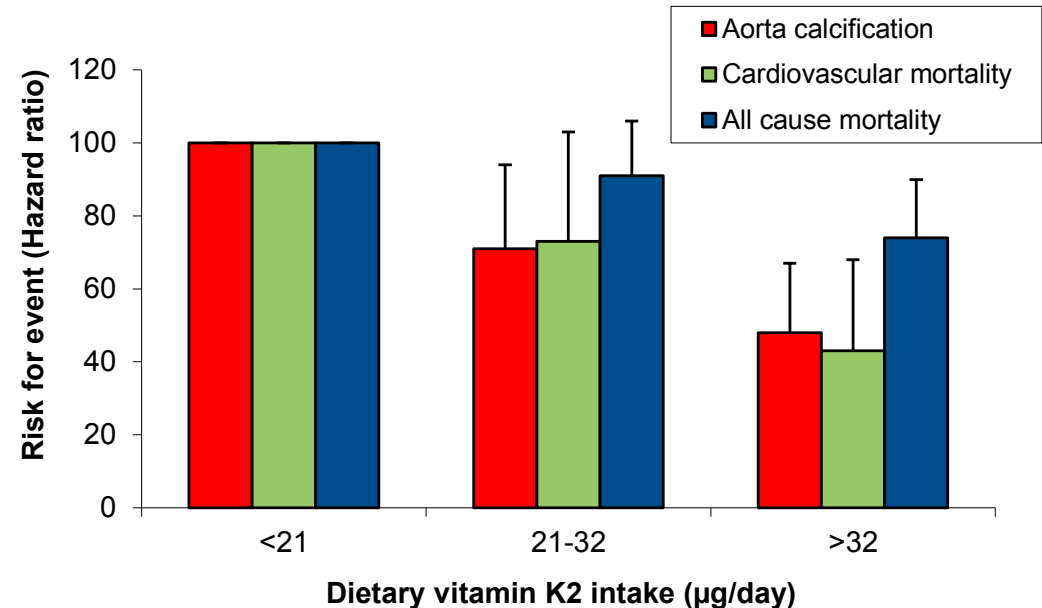
10377 asymptomatic individuals (♀ & ♂) referred by GP to coronary artery calcium screening in the US. 5 years follow-up for all-cause mortality

MenaQ7 helps decrease dp-ucMGP in HD patients



The Rotterdam Study: Importance of vitamin K2

- Over 4.800 people
- healthy elderly,
55 years and older
- 10 years follow-up
- Cross-sectional analysis
- **50% reduction of
arterial calcification**
- **50% reduction of
cardiovascular death**
- **25% reduction of
all cause mortality**

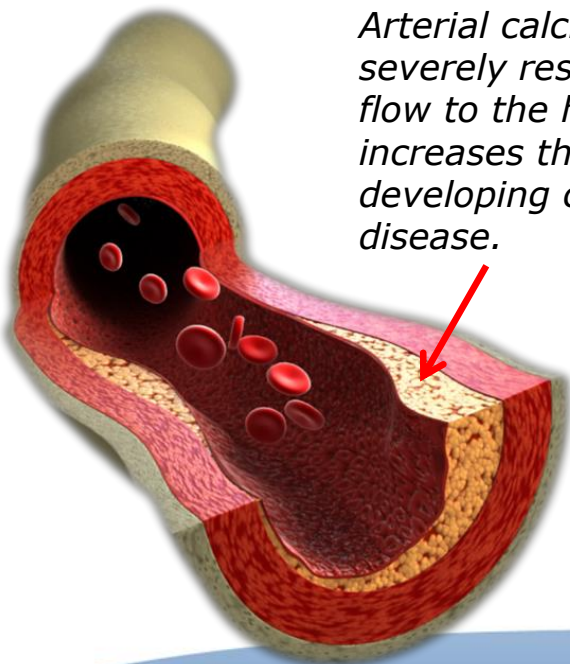


New study:

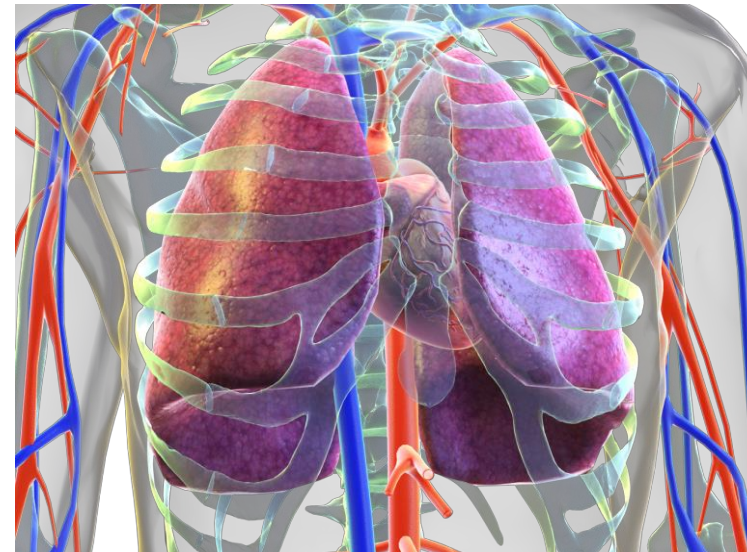
- 16,000 persons (aged 49-70)
- for every 10 µg increase in ingestion of vitamin K2 (higher menaquinones) the cardiovascular disease risk decreases by 9%. (Gast et.al, 2008)

MenaQ7[®] - Key to better heart health

- Healthy arterial tissues have been shown to contain 100 times more vitamin K2 than calcified tissues – and no K1!
- Increased consumption of natural vitamin K2 has been shown to significantly improve cardiovascular health and reduce the risk of a negative event.



Arterial calcification can severely restrict blood flow to the heart and increases the risk of developing cardiovascular disease.



General conclusions

- **New vital functions of vitamin K have been discovered not related to blood clotting**
- In all cases, vitamin K or K-related proteins play regulatory roles in important physiological processes
- **Vitamin K insufficiency of extra-hepatic tissues is widespread in healthy adults**
- No adverse effects of very high vitamin K intake have been observed
- **Increased vitamin K2 intake may improve public health and result in prolonged life expectation.**