Antioxidant and immune effects of vitamin K2

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51421

Source
ToetsingOnline

Brief title
ProteK2t study

Condition

- Other condition

Synonym
antioxidant effects, immune modulation

Health condition

Antioxidant and immune modulation in healthy subjects

Research involving
Human

Sponsors and support

Primary sponsor: Kappa Bioscience AS
Source(s) of monetary or material Support: Kappa Bioscience

Intervention

Keyword: Antioxidant, Immune function, Vitamin K2

Outcome measures

Primary outcome

To investigate the dose dependent effect of 3-week intervention with vitamin K2 (MK-7) on oxidative damage to lipids by measuring Serum oxidized LDL particles (OxLDL) in healthy, overweight men and (postmenopausal) women

Secondary outcome

To investigate the dose dependent effect of 3-week intervention with vitamin K2 (MK-7) on serum Malondialdehyde (MDA) levels in healthy, overweight men and (postmenopausal) women;

To investigate the dose dependent effect of 3-week intervention with vitamin K2 (MK-7) on serum hsCRP and IL6 levels in healthy, overweight men and (postmenopausal) women;

To investigate the dose dependent effect of 3-week intervention with vitamin K2 (MK-7) on the phagocytotic capacity, as detected in whole blood, in healthy, overweight men and (postmenopausal) women;

To investigate the dose dependent effect of 3-week intervention with vitamin K2

(MK-7) on gene expression in PBMC in healthy, overweight men and

(postmenopausal) women;

Study description

Background summary

Vitamin K is a family of naphthoquinone compounds comprising K1 (phylloquinone) and several forms of K2 (MKs, menaquinones). Phylloquinone is synthesized exclusively by plants, algae, and some species of cyanobacteria. Menaquinones are mainly produced by obligate and facultative anaerobic bacteria.
The difference in structure between K1 and K2 is seen in different absorption rates, tissue distribution, and bioavailability. Vitamin K has been first reported for its role as a cofactor for the microsomal enzyme γ-glutamyl carboxylase (GGCX) ensuring the correct function of vitamin K-dependent hepatic clotting factors. Although differing in structure, both, K1 and K2 act as cofactor for the enzyme GGCX.,
More recently, a novel role has been disclosed for vitamin K as an antioxidant and anti-inflammatory factor, independent of its activity as a cofactor for GGCX.
The number of clinical studies aiming to evaluate the benefits of the use of vitamin K2 supplementation in modulating oxidative stress and inflammation is still limited. To further evaluate these beneficial effects, including their mechanism of action, additional clinical studies are required.

Study objective

The objective is to obtain insight into a dose-dependent effect of vitamin K2 on oxidative stress and specific markers of the immune system.
The primary objective is to investigate the effect of vitamin K2 on oxidative damage to lipids by measuring oxidized LDL particles (OxLDL) in plasma in an older population.
One of the secondary objectives of the study is to investigate the effect of vitamin K2 on a second marker for oxidative stress, Malondialdehyde (MDA) in blood, as supportive evidence for protection from oxidative damage. The other secondary objectives study the effect of vitamin K2 intake on markers for immune function including: serum levels of hsCRP and IL6, the phagocytotic capacity in whole blood, and the gene expression in PBMC.

Study design

The study is designed as a randomized, double blinded, placebo controlled, 3 way crossover trial for evaluating the effect on oxidative stress markers. The

first study period, is also used as a parallel study for studying the effect on immune markers.

Intervention

All subjects in this study, will consume 333 µg vitamin K2, 666 µg vitamin K2 and placebo daily for 3 weeks. Each subject will receive each treatment for a period of 3 weeks with a 3 weeks washout period between treatments.

Study burden and risks

For this study healthy volunteers are selected. There is no direct benefit from participation, although volunteers will be reimbursed for their time investment. In total the subjects will visit the research lfacility7 times (first visit is screening visit). There are no known risks associated with the consumption of the test products.

Each subject will receive each treatment/ test product for a period of 3 weeks with a 3 weeks washout period between treatments. There are restrictions with respect to eating, drinking, and physical activity during the test days and on the pre-test days.

A faecal sample will be collected twice and blood will be drawn during each visit to the research facility (7 times). Collection of the stool or blood sample may be experienced as stressful by some people. By informing people well, we try to support them in predicting the burden and defining whether this burden is acceptable to them.

The risk associated with participation in this study is considered minimal.

Contacts

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NO

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age >=50 and <=75;
• Self-reported postmenopausal (at least one year after the final menstruation)
• BMI >=25 and <=32 kg/m2;
• Plasma dp-ucMGP concentration in highest 50-66% of the screened population
• Non-smoking (defined as not smoking currently and not having smoked (at all) in the year before study start);;
• Healthy as assessed by health questionnaire (*Gezondheidsvragenlijst*) and according to the judgment of the study physician;
• Voluntary participation;
• Having given written informed consent;
• Willing to comply with study procedures;
• Accept use of all encoded data, including publication, and the confidential use and storage of all data for 15 years;

Exclusion criteria

• Plasma dp-ucMGP concentration >1000 pmol/L at screening
• Treatment with oral antibiotics within 2 months of the start of the study
• Any vaccination in the month before study start or any scheduled vaccination during the study period
• Use of antioxidant or vitamin K and D supplements;
• Use of antioxidant or vitamin K and D supplements in the 3 months before the start of the study;
• Use of aspirin or medication with established antioxidant or anti-inflammatory properties;

• Use of medication that interferes with vitamin K or blood coagulation;
• Use of statins to reduce level of low-density lipoprotein cholesterol in the blood;
• Hyperlipidaemia, diabetes, hypertension, intestinal disease, diseases with an inflammation component;
• Hormone replacement therapy in women;
• Follow a vegetarian or vegan diet;
• Participation in any clinical trial including blood sampling and/or administration of substances up to 30 days before day 1 of this study;
• Alcohol consumption for men > 28 units/week and >4/day; for women: >21 units/week and >3/day;
• Reported unexpected weight loss or weight gain of > 3 kg in the month prior to pre-study screening, or intention to lose weight during the study period;
• Reported slimming or medically prescribed diet;
• Recent blood donation (<1 month prior to Day 01 of the study);
• Not willing to give up blood donation during the study;
• Personnel of NIZO food research, EB Medical Research and Kappa Bioscience, their partner and their first and second degree relatives;
• Not having a general practitioner;
• Not willing to accept information-transfer concerning participation in the study, or information regarding his or her health, like laboratory results and eventual adverse events to and from his general practitioner

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-12-2022
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	23-05-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-09-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-01-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL80827.028.22