Comparison of absorption and efficacy of 3 different menaquinone-7 delivery systems; casein powder, Arabic gum powder, or linseed oil.

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

Summary

ID

NL-OMON32459

Source
ToetsingOnline

Brief title
Arabic gum - absorption study

Condition

- Other condition

Synonym
Osteoporosis and vascular calcifications

Health condition

Preventie van osteoporosis en arteriosclerosis

Research involving

Human

Sponsors and support

Primary sponsor: VitaK
Source(s) of monetary or material Support: VitaK bv

Intervention

Keyword: Absorption, Arabic gum, Efficacy, Menaquinone-7 (MK-7)

Outcome measures

Primary outcome

The main purpose of the study is to compare the absorption of MK-7 from casein capsules (conventional MK-7 delivery system), Arabic gum capsules (alternative MK-7 delivery system), and linseed oil capsules in healthy subjects. The primary endpoint will be the serum level of MK-7.

Secondary outcome

The second purpose of the study is to determine the biological functionality of the different delivery systems. Therefore, the secondary endpoint will be the level of several circulating biochemical markers (cMGP, ucMGP, cOC, ucOC).

Study description

Background summary

The two most important forms of vitamin K are phylloquinone (vitamin K1) and the group of K2 vitamins (menaquinones, MK-n). In previous studies, the different forms of vitamin K have been compared with respect to their intestinal absorption, biologic half-life time, and their effect on a number of circulating biochemical markers. These studies have suggested that menaquinone-7 (MK-7) is the most effective form of vitamin K (1). MK-7 is a natural product that is found in cheese, curd, and the Japanese food natto. Supplementation studies have shown the importance of vitamin K1 as well as menaquinone-4 (MK-4) for optimal bone health and vascular health. Effects have

been reported at pharmacological doses ranging between 1 and 45 mg/d (2, 3). However, no clinical data on the health effects of MK-7 are presently available. Based on its longer half-life time and extra-hepatic tissue distribution, similar effects are to be expected with MK-7 in nutritional doses as compared to K1 and MK-4 in pharmacological doses (1). Therefore, MK-7 is recommended as the obvious choice for enrichment of dietary supplements and functional foods to improve well-being and health.
For dietary supplements, the choice of delivery vehicle is important in order to achieve maximal absorption. So far, casein (*80% of proteins in cow*s milk)-enriched powder has been used routinely for MK-7 delivery. However, cow*s milk allergy is the most common cause of food allergy affecting a minimum of 2-3% of infants. To overcome this problem, we will compare this protein-delivery system to an alternative delivery system (Arabic gum; 98% polysaccharides).
Arabic gum is widely used in both the pharmaceutical and food industries as an emulsifier and stabilizer of various products for human consumption (4). Arabic gum also has pharmacologic effects related to the gastrointestinal absorption of nutrients. It enhanced zinc absorption when orally administered in isotonic solutions to animals (5). In a rat model of chronic osmotic diarrhea, Arabic gum showed pro-absorptive properties by increased sodium and water absorption (6, 7). Our hypothesis is that the absorption of MK-7 from Arabic gum will not be significantly different from its absorption from casein.
The difference in absorption of MK-7 between powder and oil is currently unknown. We will therefore also investigate the difference between powder and oil as MK-7 delivery system. Our hypothesis is that the absorption of MK-7 from powder will not be significantly different from its absorption form oil.
To test these hypotheses, we will determine serum MK-7 concentrations to compare the absorption profiles between the different delivery vehicles. In addition, several circulating biochemical markers (cMGP, ucMGP, cOC, ucOC) will be measured to determine the biological functionality of these delivery systems. Previous research (unpublished data) indicated that 8-wk treatment of MK-7 (90 µg/d) significantly influenced the carboxylation of these biochemical markers. In addition, serum ETP levels will be measured to investigate possible effects on coagulation.

Study objective

The main purpose of the study is to compare the absorption of MK-7 from casein capsules (conventional MK-7 delivery system), Arabic gum capsules (alternative MK-7 delivery system), and linseed oil capsules in healthy subjects. The primary endpoint will be the serum level of MK-7.

Study design

The study will be a randomized, double-blind, parallel study. Sixty-nine healthy men and women between 20 and 40 y will be recruited in the southern

region of Limburg. Before the actual start of the study and after an initial informative meeting, a screening (= blood sampling) will take place to select subjects with a low vitamin K status [marker = ucMGP; min cutoff value of 60 pmol/L (8)]. Eligible participants will be randomly divided over 3 treatment groups to receive either casein capsules, Arabic gum capsules, or linseed oil capsules. All capsules will be enriched with MK-7 (90 µg/d).
• Group 1: 20 subjects will receive daily 1 casein capsule (MK-7 intake = 90 µg/d).
• Group 2: 20 subjects will receive daily 1 Arabic gum capsule (MK-7 intake = 90 µg/d).
• Group 3: 20 subjects will receive daily 1 linseed oil capsule (MK-7 intake = 90 µg/d).
A first blood sample will be taken after an overnight fast (t = 0 h) on the first test day. Next, the participants will consume the capsules (1 capsule/subject) together with a standard breakfast [including fat, carbohydrates, and protein; 3 slices of brown bread with chocolate paste or margarine and jam, and 2 glasses of milk (milk or fruit&milk beverage)]. The subsequent samples will be taken at the first test day (t = 0, 2, 4, 6, and 8 h) and several follow-up days (t = 1, 4, and day 7) to determine the absorption profile. Starting from day 8, subjects will take daily 1 capsule together with breakfast during the remaining 7 weeks of the study. Blood sampling will be taken at days 14, 28, 42, and 56 to determine the biological functionality of MK-7.

Intervention

Participants will be randomly divided to receive; casein capsules (1 capsule/d), Arabic gum capsules (1 capsule/d), or linseed oil capsules (1 capsule/d). All capsules will be enriched with 90 µg MK-7. One week before the start of the study and during the 8-wk treatment, participants will be asked to refrain from consuming foods rich in vitamin K, including both K1-rich foods (e.g. spinach, kale, broccoli, Brussels sprouts) and MK-rich foods (e.g. curd cheese, cheese, natto).

Study burden and risks

One week before the start of the study and during the 8-wk treatment, participants will be asked to refrain from consuming foods rich in vitamin K, including both K1-rich foods (e.g. spinach, kale, broccoli, Brussels sprouts) and MK-rich foods (e.g. curd cheese, cheese, natto).
The major burden for the subjects will consist of 13 venipunctures during the 8-wk study (fasting state). The venipunctures will be made by experienced coworkers. Nevertheless, blood sampling may cause bruising or hematoma. The daily dose of MK-7 (90 µg) will not cause adverse side-effects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Healthy men and women aged between 20 and 40 y
• Normal body weight and height (BMI <30 kg/m2)
• Stable body weight (weight gain or loss <3 kg in past 3 mo)
• Written consent to take part in the study
• Low vitamin K status (will be checked during the screening and not the informative meeting)

Exclusion criteria

• (A history of) metabolic or gastrointestinal diseases
• Chronic degenerative and/or inflammatory diseases

• Abuse of drugs and/or alcohol
• Use of corticosteroids
• Use of oral anticoagulants
• (A history of) soy, milk, or natto allergy
• Use of vitamin K-containing multivitamins or vitamin K supplements
• Anaemia
• Blood donation or participation in another study within one month before the study

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2008
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	29-10-2008
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL24747.068.08
Other	Zal geregistreerd worden via www.clnicaltrials.gov