

Milk products supplemented with Phytosterols or omega-3 oils and biomarkers of cardiovascular disease

Submission date 14/03/2017	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 16/03/2017	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 18/06/2025	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

A high blood cholesterol level (hypercholesterolemia) causes an increased risk of cardiovascular (heart) disease, as cholesterol can build up in the arteries and lead to a myocardial infarction (heart attack). Diet changes are a useful strategy for the prevention of many diseases, especially those in which obesity is a risk factor, including cardiovascular disease. Phytosterols are vegetable substances similar to human cholesterol, but consuming them can control and even lower blood cholesterol levels. Similarly, omega-3 fatty acids, substances naturally found in fish and breast milk, have also been found to prevent cardiovascular disease. The aim of this study is to find out whether the daily intake of milk products enriched in phytosterols and omega-3 fatty acids can help prevent cardiovascular disease.

Who can participate?

Healthy adults between 25 and 70 years old who are overweight or obese

What does the study involve?

The study consists of two 28-day periods separated by a 4-week break. Participants are randomly allocated to one of two groups. The first group drink phytosterol-enriched milk in the first period and omega-3-enriched milk in the second period. The second group drink omega-3-enriched milk in the first period and PhyS-enriched milk in the second period. During the 2 weeks before the start of the study and the 4-week break, participants in both groups drink commercially available plain low-fat milk (without phytosterol or omega-3). All participants are requested to maintain their normal diet and physical activity throughout the study. Participants provide blood samples before and after each of the two periods to find out whether their cholesterol levels are affected.

What are the possible benefits and risks of participating?

The results of this study may show why regular intake of phytosterols and omega-3 fatty acids has health benefits. However, the individual participant may not benefit. There are no expected risks of participating in this study, except from the discomfort of blood sampling.

Where is the study run from?

Instituto Catalán de Ciencias Cardiovasculares (ICCC) - Hospital de la Santa Creu i Sant Pau (Spain)

When is the study starting and how long is it expected to run for?

February to July 2012

Who is funding the study?

1. Ministerio de Economía y Competitividad (Spain)

2. Instituto de Salud Carlos III (Spain)

Who is the main contact?

1. Prof. Lina Badimon

2. Dr Teresa Padro

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

ICCC-9 FITOCARD

Study information

Scientific Title

Scientific basis of cardiovascular effects derived from the regular consumption of milk products supplemented with Phytosterols or omega-3 oils at systemic level in subjects at low cardiovascular risk with moderated hypercholesterolemia and overweight or obesity.

Acronym

FITOCARD

Study objectives

The main objective of this study is to characterize the differential proteomic profile and the lipidic profile of serum and plasma samples from healthy volunteers after the intake of a regular plain milk supplemented with either Phytosterols or Omega-3 fatty acids and to identify changes on any biomarker associated to the prevention of the cardiovascular risk.

Hypothesis: Low-fat milks supplemented with Phytosterols or long-chain n-3 PUFA have health benefits beyond their efficacy as lipid-lowering agents. Beneficial effects are evidenced through changes in plasma lipidomic and proteomic profiles as well as gene expression in peripheral blood cells that predisposes to lower cardiovascular risk. No adverse events will be observed.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics Committee for Clinical Research from the Hospital de la Santa Cruz y San Pablo, 05/07 /2011, ref: 10/2011

Study design

Double-blind randomized two-arm longitudinal crossover study

Primary study design

Interventional

Secondary study design

Randomised cross over trial

Study setting(s)

Hospital

Study type(s)

Prevention

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Arteriosclerosis

Interventions

All subjects were submitted to two 28-day treatment sequences, separated by a 4 weeks washout period. Before the initiation of the intervention, individuals were submitted to a 2-week run-in period. During the run-in and wash-out periods, participants received 250 mL/day commercially available plain low-fat milk (without PhyS or ω -3), with the same composition to that used for preparing the PhyS-enriched- and ω -3 enriched milks.

At the end of the run-in period, subjects were randomly allocated to receive one of the two treatment sequences:

Study arm 1: Phytosterol (PhyS)-enriched milk in the first intervention period and ω -3 enriched milk in the second intervention period

Study arm 2: Omega-3 (ω 3)-enriched milk in the first intervention period and PhyS-enriched milk in the second intervention period

Participants were instructed to consume a pack of milk (250 mL) per day, distributed in one or more portions according to their normal habits, replacing their habitual milk-products consumption. Subjects were requested to maintain their habitual diet at levels consistent with maintenance of a stable body weight and to continue their normal pattern of physical activity throughout the study period.

Lipid content varied from 0.4 g per 100 mL milk in the control low-fat milk to 0.8 g in the ω 3-enriched milk and 0.9 g in the PhyS-enriched milk. The 20.6% of the lipid content in the ω 3-enriched milk were omega-3 fatty acids, mainly consisting in EPA and DHA (150 mg EPA+DHA / 100 mL milk) that represented the 90.8% of the total omega-3 fatty acid content. In addition to lipid content, every 100 mL PhyS-enriched milk contained 0.64 g plant sterols (expressed as free PhyS). According to the provider's information, the supplemented vegetable oil-based sterols (VEGAPURE® 95E) were mainly found as sterol esters (>94%) with 68% poly-unsaturated FA (C 18:2), 19% monounsaturated FA (18:1), and 13% saturated FA (16:0, 18:0). PhyS mix mainly consisted of sitosterol, campesterol, and stigmasterol (>77%), being sitostanol and campestanol the more abundant stanols. The content in other sterols/stanols did not exceed the 3%.

Intervention Type

Supplement

Primary outcome measure

1. Triglyceride and cholesterol levels, measured using biochemical analysis
2. Oxidative profile: measure of the lipidic peroxidation in plasma and LDL, the plasma antioxidant behavior and LDL resistance to oxidation
3. Fatty acids (FA) and lipidomic pattern measured in plasma and LDL samples respectively and

analyzed by LC/MS/MS. The analysis of FA is performed after the derivatization of the samples to convert FAs into thrimethylaminoethyl ester iodide derivatives. LDL lipidomic profile is analyzed in mixture with an internal lipid standard mixture

4. Proteomic profile:

4.1. Analysis of the differential proteomic profile of the lipid and lipid-free fraction of serum and plasma samples measured by 2DE electrophoresis, followed by protein identification by mass spectrometry identification (MALDI-TOF)

4.2. Validation of the results by western blot analysis and enzyme-linked immunosorbent assay (ELISA) kits

Measured at baseline and after each intervention period

Secondary outcome measures

1. Alcohol intake, smoking and dietary habits, taken from participants' medical records

2. Dietary habits, assessed using a questionnaire at baseline

3. Inflammatory variables related to atherosclerosis

4. Gene expression measured by RT-PCR and arrays either in the plasma or the blood cellular fraction after the intake of supplemented milk

5. Circulating microparticles assessed using blood samples or the cells of the vascular wall

6. Potential gene polymorphisms associated with the response to the interventions at proteomic and lipidomic levels

Measured at baseline and after each intervention period

Overall study start date

15/02/2012

Completion date

20/07/2012

Eligibility

Key inclusion criteria

1. Healthy adult males and females between 25 and 70 years old

2. Overweight or grade 1 obese (body mass index greater than 25 kg/m²)

3. Signed informed consent

Participant type(s)

Healthy volunteer

Age group

Adult

Sex

Both

Target number of participants

35 participants (10% loss is accepted)

Total final enrolment

32

Key exclusion criteria

1. Previous history of cardiovascular disease (ischaemic heart disease - angina or recent or old myocardial infarction, cerebral vascular accident, or peripheral vascular disease)
2. No documented cardiovascular disease (ischaemic heart disease - angina or recent or old myocardial infarction or previous or cerebral vascular accident, peripheral vascular disease)
3. Any disease affecting lipid metabolism
4. Any severe chronic disease
5. Lactose intolerance
6. Being in the phase of weight loss or expressing a desire for weight loss in the 4 months of the study
3. Alcohol consumption >60 g/day
7. Under treatment with fibrates or statins

Date of first enrolment

15/02/2012

Date of final enrolment

14/03/2012

Locations**Countries of recruitment**

Spain

Study participating centre

Instituto Catalán de Ciencias Cardiovasculares (ICCC) - Hospital de la Santa Creu i Sant Pau

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Sponsor information**Organisation**

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Sponsor details

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Sponsor type

Research organisation

ROR

<https://ror.org/059n1d175>

Funder(s)

Funder type

Government

Funder Name

Ministerio de Economía y Competitividad

Alternative Name(s)

Ministry of Economy and Competitiveness, MINECO, MEC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Spain

Funder Name

Instituto de Salud Carlos III

Alternative Name(s)

SaludISCI, Instituto de Salud Carlos III, Instituto de Salud Carlos III | Madrid, Spain, Carlos III Institute of Health, Institute of Health Carlos III, Carlos III Health Institute, ISCI

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Spain

Results and Publications

Publication and dissemination plan

1. The results will be presented at the annual congress covering atherosclerosis, nutrition and biomarkers, as well as in novel omic technologies.
2. Three different publications are planned. These will specifically address the following areas: the lipid/lipidomic studies, the proteomic study, and the study on microparticles

Intention to publish date

16/03/2019

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Teresa Padró

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2015		Yes	No
Results article		13/06/2017	26/04/2023	Yes	No
Other publications	Exploratory sub-study	18/08/2023	18/06/2025	Yes	No