

Virgin olive oil and high-density lipoprotein functionality: a model for tailoring functional food

Submission date 06/03/2012	Recruitment status No longer recruiting	☐ Prospectively registered
		☐ Protocol
Registration date 09/05/2012	Overall study status Completed	☐ Statistical analysis plan
		☒ Results
Last Edited 25/04/2016	Condition category Nutritional, Metabolic, Endocrine	☐ Individual participant data

Plain English summary of protocol

Background and study aims

The aim of this study is to find out whether consuming olive oil enriched with olive oil phenolic compounds (OOPC) and olive oil enriched with OOPC plus flavonoids from thyme increases quality and quantity of high density lipoprotein (HDL) compared with consuming normal virgin olive oil.

Who can participate?

Male and female hypercholesterolemic (>200mg/dL) patients aged 20-80 years.

What does the study involve?

Participants will receive 25 ml per day of one of the three types of olive oil in three separate periods of 3 weeks, preceded each one by a 2-week wash-out period.

What are the possible benefits and risks of participating?

The benefit for the participants will be the possibility of reducing their cardiovascular disease risk. No harmful effects have been found to be associated with olive oil consumption.

Where is the study run from?

Institut Hospital del Mar d'Investigacions Mèdiques (IMIM) , Barcelona, Spain

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

April to September 2012

Who is funding the study?

Spanish Ministry of Economy and Competitiveness

Who is the main contact?

Dr María-Isabel Covas

mcovas@imim.es

mfito@imim.es

Contact information

Type(s)

Scientific

Contact name

Dr Maria Isabel Covas

Contact details

Doctor Aiguader, 88

Barcelona

Spain

08003

+34 (0)933 160 720

mcovas@imim.es

Additional identifiers

Protocol serial number

AGL2009-13517-C03-01

Study information

Scientific Title

Virgin Olive oil and HDL Functionality (VOHF): a model for tailoring functional food: the VOHF project

Acronym

VOHF

Study objectives

A flavoured functional olive oil enriched not only with its own phenolics but also with complementary ones (regarding structure/function) from thyme could provide additional health benefits and consumers acceptance.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Clinical Research Ethical Committee of the "Institut Municipal dAssistència Sanitària (IMAS)", 09/09/2009, ref: 2009/3347/I

Study design

Randomized controlled double-blind cross-over single-centre clinical supplementation trial

Primary study design

Interventional

Study type(s)

Quality of life

Health condition(s) or problem(s) studied

Hypercholesterolemic patients

Interventions

Current interventions as of 23/04/2014:

Randomized, controlled, double-blind, cross-over, single-centre clinical supplementation trial, in which 33 subjects (19 men and 14 women) will be randomised to one of 3 orders of administration of 25 ml/day of raw:

1. Virgin olive oil (Control)
2. Functional Olive Oil 1 enriched with its own phenolic compounds (FOO1)
3. Functional Olive Oil 2 enriched with its olive oil phenolic compounds plus those of thyme (FOO2)

This will be in 3 periods of 3 weeks

Previous interventions:

Randomized, double-blind, cross-over, single-centre clinical supplementation trial, in which 30 subjects (15 men and 15 women) will be randomised to one of 3 orders of administration of:

1. 25 mL/day of raw refined virgin olive oil (Control)
2. Functional Olive Oil 1 enriched with its own phenolic compounds (FOO1)
3. Functional Olive Oil 2 enriched with its olive oil phenolic compounds plus those of thyme (FOO2)

This will be in 3 periods of 3 weeks

Intervention Type

Supplement

Primary outcome(s)

1. HDL functionality:

The following parameters will be measured at baseline and before and after each intervention:

- 1.1. Markers of compliance: Measurement of tyrosol and hydroxytyrosol in spot morning urine will be performed by GC/mass spectrometry
- 1.2. Parameters of HDL functionality: Isolation of HDL will be done by sequential centrifugation.
2. The following parameters will be measured in isolated HDL:
 - 2.1. Fatty acid content, vitamin E, and total phenolic content in HDL by HPLC-DAD
 - 2.2. Apolipoproteins (Apo)A1, ApoA2, and ApoA4 by ELISA
 - 2.3. Cholesterol esther transfer protein (CETP) and lecithine cholesterol acyl transferase (LCAT) by fluorometry
 - 2.4. Paraoxonase (Organophosphatase activity) PON1) and PAF-AH activities by spectrometry with automated mode
 - 2.5. 3 chlorotyrosine and 3-nitro-tyrosine by GC/MS
 - 2.6. Bilayer fluidity of HDL will be measured by confocal microscopy. Cholesterol efflux from cells will be measured in culture of macrophages.
3. OMICS

Gene expression assay will be performed as previously described. Several candidate genes implicated in the increase of the HDL cholesterol and in the improvement of the HDL

functionality in humans will be tested. Candidate genes: ABCA1: ATP-binding cassette, sub-family A (ABC1), member 1; ABCG1: ATP-binding cassette, sub-family G (WHITE), member 1; and ABCG4: ATP-binding cassette, sub-family G (WHITE), member 4 ApoA1: apolipoprotein A- I; and ApoE: apolipoprotein E; LPL: lipoprotein lipase; PAF-AH1B3: platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit 29kDa; PPARalpha: peroxisome proliferator - activated receptor alpha; PPARgamma: peroxisome proliferator-activated receptor gamma; and PBPPAR: PPAR binding protein; RARA: retinoic acid receptor, alpha. Proteomic analyses, by separation with 2-DE (two-dimensional gel electrophoresis) and PMF (protein mass fingerprinting) with MALDI-TOF-MS (matrix -assisted laser desorption/ionization time of flight mass spectrometry ,will be performed in plasma samples.

Key secondary outcome(s)

Oxidative damage

The following parameters will be measured at baseline and before and after each intervention:

1. Plasma lipids will be performed by enzymatic methods in a automated mode. In vivo circulating oxidized LDL and 3 chlorotyrosine derivatives in urine will be determined by ELISA
2. Protein carbonyl content (PCC) by spectrometry
3. 8-isoprostane (8-epi PGF2 α)
4. 8-hydroxydeoxyguanosine (8-OHdG) by enzyme-linked immunosorbent assay (ELISA)

Added 23/04/2014:

5. Endothelial function
6. Intestinal microorganism study

Completion date

07/09/2012

Eligibility

Key inclusion criteria

Current inclusion criteria as of 23/04/2014:

1. Hypercholesterolemic patients (>200 mg/dL)
2. Aged 20-80 years

Previous inclusion criteria:

1. Hyperlipidemic patients
2. Patients with low (<40 mg/dL) HDL cholesterol
3. Aged 20-60 years

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

Current exclusion criteria as of 25/04/2014:

1. Smokers
2. Athletes with PA >3000 kcal/day
3. BMI >35 kg/m²
4. Diabetes, multiple allergies, intestinal diseases
5. Any condition that limits the mobility of the subject making study visits impossible
6. Life threatening illness such as cancer or severe disease with a lowered expected 3 year survival
7. Any other disease or condition that would worsen the adherence to the measurements or treatment

Previous exclusion criteria:

1. Intake of antioxidant supplement or acetylsalicylic acid or any other drug with established antioxidative properties
2. Athletes with PA >3000 kcal/week in leisure-time
3. Obesity (BMI > 30 kg/m²)
4. Diabetes, multiple allergies, intestinal diseases
5. Any condition that limits the mobility of the subject making study visits impossible
6. Life threatening illness such as cancer or severe disease with a lowered expected 3 year survival
7. Any other disease or condition that would worsen the adherence to the measurements or treatment

Date of first enrolment

02/04/2012

Date of final enrolment

07/09/2012

Locations

Countries of recruitment

Spain

Study participating centre

Doctor Aiguader, 88

Barcelona

Spain

08003

Sponsor information

Organisation

Spanish Ministry of Economy and Competitiveness (Spain)

Funder(s)

Funder type

Government

Funder Name

Spanish Ministry Science and Technology (Spain) ref: AGL2009-13517-C03-01

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	10/06/2015		Yes	No