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Bioavailability and effects of soluble phenols of cocoa on inflammatory biomarkers related to atherosclerosis

Submission date 04/05/2009	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/06/2009	**Overall study status** Completed	
Last Edited 16/05/2013	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
AGL2004-08378-C02-02/ALI

Study information

Scientific Title
Bioavailability of soluble phenols of cocoa. Scientific basis of the interaction of phenolic compounds and cellular and serum inflammatory biomarkers related to atherosclerosis: an open randomised cross-over controlled trial

Study objectives
Soluble polyphenolic compounds of cocoa powder will reduce inflammatory biomarkers related to atherosclerosis. No adverse events will be observed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of the Hospital Clínic de Barcelona, approved on the 3rd June 2003.

Study design
Open randomised cross-over controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Arteriosclerosis

Interventions
Initial wash-out period (15 days) followed by first intervention (28 days) and second intervention (28 days).

Intervention 1: 40 g/day of soluble cocoa powder dissolved in 250 mL of skim milk
Intervention 2: 250 mL of skim milk daily

There was no wash-out period between the two interventions. Since the period of each intervention was four weeks and the change of the variables studied occurred <15 days, we assumed that we can evaluate the effects of both interventions, comparing the results of the analysis performed at the end of each intervention.

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Cocoa

Primary outcome measure
1. Leukocyte adhesion molecule expression
Lymphocyte and monocyte adhesion molecules on these cells will be marked with monoclonal antibodies (MAb) conjugated with fluorescein-isothiocyanate (FITC) and phycoerythrin (PE) by direct double immunofluorescence. The MAb of the adhesion molecules used will be: anti-CD11a (LFA-1), anti-CD40L, anti-CD11b (Mac-1) (Bender MedSystems Diagnostics, Austria), anti-Syalil Lewis (anti-CD15s) (Pharmingen, USA), anti-CD49d (VLA-4) (Cytogmos, Spain). The monoclonal antibodies used to mark the T-lymphocytes will be anti-CD2 and monocytes, anti-CD14 (Caltag Laboratories, USA).
2. Soluble adhesion molecules
The following serum soluble adhesion molecules will be determined by enzyme-linked immunosorbent assay (ELISA) kits: C-reactive protein (CRP), sICAM-1, sVCAM-1, sE-selectin, and sP-selectin, as well as sMCP-1, and IL-6 (Immunotech, Czech Republic).
3. Nuclear factor kppa B by western blot of peripheral blood mononuclear cells
4. Bioavailability of soluble phenolic compounds of cocoa powder by Liquid Chromatography /Mass Spectrometry/Mass Spectrometry (LC-MS/MS) analysis of plasma and urine metabolites

All outcomes will be measured at baseline and after each intervention period.

Secondary outcome measures
1. Medical record
A complete medical record will be obtained from all participants, which included data on cocoa intake, smoking and dietary habits. Blood pressure and heart rate will be measured with an electronic apparatus Omron HEM-705CP (Netherlands).
2. Nutrition assessment and general analyses
All participants will complete a validated nutritional questionnaire at baseline to determine the total quantity of calories ingested in the previous month as well as the proportion corresponding to carbohydrates, lipids and proteins. Overall nutrition will be determined by percentage of ideal weight, lean body mass and body mass index. Waist perimeter will be measured. The proteic nutrition will be determined on the basis of the following parameters: haemoglobin, total lymphocyte count, total proteins, albumin, prealbumin, transferrin and retinol-binding protein. Serum and intraerythrocytary folic acid concentrations will be measured, as well as serum vitamin A, B1, B12, C, E, B-carotenes, Zn, Mg and Se concentrations.
Moreover, the following measurements will also be obtained: red blood cell count, hematocrit, mean corpuscular volume, leukocyte count, glucose, creatinine, electrolytes, uric acid, transaminases, lactate dehydrogenase, alkaline phosphatase, gammaglutamyl transpeptidase and bilirrubin.
3. Coagulation tests
The following parameters will also be determined: platelet count, prothrombin time, and plasma fibrinogen.
4. Serum lipoproteins and others
Total cholesterol, triglycerides, cHDL, cLDL, Apo A1, Apo B, lipoprotein (a) and homocysteine will be determined.

5. Diet and exercise monitoring
All participants will follow an isocaloric diet prepared according to their personal preferences. Subjects will be asked to exclude all other cocoa-containing foods throughout the study and to limit the intake of foods containing high polyphenol content, such as virgin olive oil, red wine, tea, fruits, and vegetables. The diet will be strictly monitored during the study. Diet compliance will be assessed from 3-days (2 weekdays and 1 weekend day) diet records administered before each evaluation. This assessment will be administered by trained personnel. The foods ingested will be converted into nutritional values with the aid of the Professional Diet Balancer software (Cardinal Health Systems, Inc., USA). Physical activity will also be evaluated with the Minnesota Leisure Time Physical Activity questionnaire which has also been validated in Spain. Control of the diet and physical exercise will be carried out before and after each intervention, the same day on which the clinical examinations are performed and blood is withdrawn for immunologic studies.

All outcomes will be measured at baseline and after each intervention period.

Overall study start date
01/12/2004

Completion date
01/12/2007

Eligibility

Key inclusion criteria
1. Males and females between 55 and 80 years old
2. Those without documented cardiovascular disease (ischemic heart disease, stroke, or peripheral vascular disease)
3. Those who have diabetes mellitus or two or more of the following factors:
3.1. Current smoking
3.2. Hypertension
3.3. Hypercholesterolemia (low-density Lipoprotein [LDL]-cholesterol >160 mg/dl)
3.4. High-density lipoprotein (HDL)-cholesterol <40 mg/dl
3.5. Obese (body mass index >30 kg/m^2)
3.6. Family history of premature coronary heart disease
4. Participant should give signed informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
45

Key exclusion criteria

1. Subjects with a previous history of cardiovascular disease (ischemic heart disease, stroke or peripheral vascular disease)
2. Any severe chronic disease
3. History of allergic reactions to any cocoa or milk components

Date of first enrolment
01/12/2004

Date of final enrolment
01/12/2007

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Clínic de Barcelona
Barcelona
Spain
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Sponsor information

Organisation
Ministry of Science and Innovation (Ministerio de Ciencia e Innovación) (Spain)

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Sponsor type
Government

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Funder(s)

Funder type
Government

Funder Name
Ministry of Science and Innovation (Ministerio de Ciencia e Innovación) (Spain) (ref: AGL2004-08378-C02-02/ALI)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/11/2009		Yes	No
Results article	results	01/12/2012		Yes	No