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

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

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

registered

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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

 Subjects with a previous history of cardiovascular disease (ischemic heart disease, stroke or peripheral vascular disease)
Any severe chronic disease
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 08036

Sponsor information

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

Sponsor details

C/Albacete, 5 Madrid Spain 28027

Sponsor type Government

Website http://web.micinn.es

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