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The Chocolate, Orange juice and Blackberry (COB) study

Submission date
22/07/2013

Recruitment status
No longer recruiting

Registration date
22/07/2013

Overall study status
Completed

Last Edited
25/04/2019

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
The era of general dietary recommendations for the whole population may be coming to an end, as it is becoming apparent that people do not respond in the same way to the same foods. Within a decade it is believed that individuals at risk of specific conditions will be easily identified and accordingly may be recommended personalised nutrition based on their genetic make-up. Food compounds known as flavonoids can be found in plant-based foods including fruits, tea and chocolate. The aim of this study is to determine whether the processing of flavonoids in the human body differs between individuals depending on age, gender, genetic make-up or the bacteria present in the gut.

Who can participate?
European Caucasian men and women (non-smokers) who are aged either 18-30 or 65-77 years and are generally healthy

What does the study involve?
Volunteers involved in the study first follow a dietary restriction by avoiding fruits, vegetables, wholegrain foods, tea, coffee or fruit juice for 3 days before the main study day (Day 4). On Day 4 they are asked to have a test meal consisting of a bar of chocolate and a glass of juice made from freeze dried blackberries and an extract of orange, which are rich in flavonoids. They are then be asked to provide a blood sample on Days 4 and 5 and provide urine samples on Days 3, 4 and 5. They are also asked to provide a faecal sample on either Day 3 or the morning of Day 4 before eating the test meal. All foods are provided on Days 4 and 5. The volunteers need to visit the clinical research facility a total of five times for the entire study (including a consent visit and a screening visit). Most of the visits take less than 1 hour each except for Day 4 (main study visit) which is about 8 hours long. Travel expenses are reimbursed and the volunteers receive £25 for their time.

What are the possible benefits and risks of participating?
This is a nutritional study and as such there will be no direct benefit to the participants in taking part in this study. However, the volunteers may benefit from knowing their blood chemistry and blood pressure results as part of the screening process for this study. There are no expected adverse effects of the intervention in this study, as the naturally occurring compounds are

presented in food sources readily consumed in the habitual diet and at doses which can be readily achieved through normal dietary practices. As a safeguard, participants will be asked at screening whether they have known allergy to the study foods (chocolate, orange juice, blackberries).

Where is the study run from?
Clinical Research Facility at the Medical School of the University of East Anglia, Norwich (UK)

When is the study starting and how long is it expected to run for?
July 2013 to September 2014

Who is funding the study?
Biotechnology and Biological Sciences Research Council (BBSRC) (UK)

Who is the main contact?
Prof. Anne Marie Minihane
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Study website
http://www.cobstudy.org/

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01922869

Secondary identifying numbers
14638

Study information

Scientific Title
A human acute flavonoid intervention study to examine flavonoid metabolism and the effect on memory/cognition

Acronym
COB

Study objectives
Investigation of the genetic and phenotypic determinants of flavonoid absorption and metabolism. Assessing the influence of age, sex, gut microbiota and host genetics on inter-personal differences in flavonoid metabolism.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England, Norfolk, Research Ethics Committee, ref: 13/EE/0066

Study design
Non-randomised interventional trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Participants information can be found at http://www.cobstudy.org/what-is-the-study-about

Health condition(s) or problem(s) studied
Topic: Primary Care Research Network for England; Subtopic: Not Assigned; Disease: All Diseases

Interventions
Mixed flavonoid source, food source of a mixture of flavonoids.

The study will be an acute nutritional intervention study. Volunteers will be asked to consume one dose of a flavonoid rich test meal, consisting of chocolate and a juice made from freeze dried blackberry powder and an extract of orange, providing approximately 640 mg of flavan-3-ols, 390 mg of anthocyanins and 342 mg of flavanones. The study takes 5 days in total, including 3 days of dietary restriction and 2 days of follow-up after the flavonoid rich test meal administration.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
The primary outcome measure for the study will be the measurement of the concentrations of flavonoids and their metabolites in blood and urine. They will be assessed in samples provided before the administration of the flavonoid rich test meal (24 hour pre-administration urine and a blood sample immediately before test meal administration) and several times after the test meal administration (7 regular blood samples over a 24 hour period and 2 x 24 hour urine, to be collected up to 48 hours after the test meal administration).

Flavonoids and their metabolites will be assessed using state-of-the-art liquid chromatography-tandem mass spectrometry (LC-MS/MS) and quantified against commercially available standards. Serum and urine will be acidified and then extracted by solid phase extraction (SPE). Metabolite identification will be performed using a QTrap 4000 linear ion trap mass spectrometer (ABSciex, Canada) by multi-reaction monitoring (MRM) optimized for the detection of pure standards. Metabolites will be confirmed on the basis of retention time and parent-daughter ion fragmentation transitions.

Secondary outcome measures
The secondary outcome measure for the study will be to investigate the influence of gut microbiota variation on flavonoid absorption and metabolism. To do this, we will collect faecal samples and determine gut-microflora using faecal bacterial phylogenetic analysis using PCR to amplify 16S rDNA genes. Faecal samples will be collected within 24 hours before the administration of the flavonoid rich test meal.

Overall study start date
08/07/2013

Completion date
31/07/2014

Eligibility

Key inclusion criteria
1. Men and women
2. 18-30 years or 65-77 years
3. White Caucasian, of European origin
4. Non-smokers
5. Gnerally healthy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
77 Years

Sex
Both

Target number of participants
Planned Sample Size: 240; UK Sample Size: 240; Description: 18-30yrs (n=120) and 65-77yrs (n=120). Generally healthy, caucasian and non-smoker.

Key exclusion criteria
1. Smoke
2. Are pregnant, have been pregnant in the last year or are breastfeeding
3. Have any existing medical conditions or significant past medical history likely to affect study measurements e.g., type 2 diabetes, cardiovascular, renal, liver, gastrointestinal diseases
4. Are on medication that may affect the study outcome
5. Have used antibiotics within the last three months
6. Have had vaccinations within the last three months
7. Take certain dietary supplements or herbal remedies and are unwilling to stop taking them
8. Have been involved in another research project within the last 3 months
9. Are unable to provide written informed consent
10. Have donated blood in the 16 weeks prior to the start of this study or intend to donate blood in the 16 weeks following this study
11. Have body mass index (BMI, kg/m2) <18.5
12. Have body mass index (BMI, kg/m2) >30
13. Have blood pressure < 90/60 mmHg
14. Have blood pressure > 140/90 mmHg

Date of first enrolment
08/07/2013

Date of final enrolment
31/07/2014

Locations

Countries of recruitment
United Kingdom

Study participating centre
Norwich Research Park
Norwich
United Kingdom
NR4 7 TJ

Sponsor information

Organisation
University of East Anglia (UK)

Sponsor details
Research and Enterprise Services
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Sponsor type
University/education

Website
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ROR
https://ror.org/026k5mg93

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Sciences Research Council (BBSRC) (UK) Grant Codes: BB-J004545-1

Alternative Name(s)
UKRI - Biotechnology And Biological Sciences Research Council, BBSRC UK, BBSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

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?
Abstract results	oral presentation	01/06/2014	25/04/2019	No	No
HRA research summary			28/06/2023	No	No