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The Orange Juice and Cardiovascular Disease Study

Submission date	Recruitment status	[X] Prospectively registered
25/07/2014	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/07/2014	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/06/2019	Circulatory System	

Plain English summary of protocol

Background and study aims
Anthocyanins are naturally occurring substances found in a variety of foods and drinks. They are responsible for the deep red, blue, purple and black colours of foods such as berry fruits, blood oranges and aubergine skins. Evidence suggests that anthocyanins may play a role in preventing diseases such as cardiovascular (heart) disease. The aim of this study is to look at the effects of drinking blood orange juice (with anthocyanins) and a standard blonde orange juice (without anthocyanins) on a variety of markers for cardiovascular disease risk.

Who can participate?
Healthy volunteers aged between 25 and 84 with a waist size of 40 inches or greater (men) or 34 inches or greater (women)

What does the study involve?
Participants are randomly allocated to drink up to 500mL of either blood or blond orange juice each day for 28 days, then after a 3-week break they drink the other juice for 28 days. Blood samples are collected at the start and end of each 28-day period for the measurement of markers of cardiovascular disease risk. Participants are expected to consume a diet low in anthocyanins from two weeks before starting the study and continuing throughout the study period (about 12 weeks in total).

What are the possible benefits and risks of participating?
There are no direct benefits of taking part in this study. However, the information obtained contributes to the evidence of the effects of anthocyanins on cardiovascular disease risk. Since this study involves blood sampling there can be a small amount of discomfort associated with taking blood. There is a risk that participants may develop a small bruise at the site of the blood sample but this fades as with any bruise.

Where is the study run from?
Institute of Food Research (UK)

When is the study starting and how long is it expected to run for?
August 2014 to December 2017

Who is funding the study?
European Commission (Belgium)

Who is the main contact?
Dr Charlotte Armah
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02195934

Protocol serial number
16925

Study information

Scientific Title
The Orange Juice and Cardiovascular Disease Study: a randomised controlled trial

Acronym
The OJ & CVD Study

Study objectives
This study aims to compare the effect of anthocyanin-rich blood orange juice with a standard (no anthocyanin) blonde orange juice on markers of cardiovascular disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)

First MREC approval date 24/06/2014, ref: 14/EE/0219

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Other

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

Interventions
Participants aged between 25 and 84 years of age will be recruited based on their waist measurement, with 42 participants required to complete the study. They will be required to consume up to 500mL of either blood or blond juice each day for 28 days in a two-way cross-over study. Prior to each part of the intervention there will be a 2 week run in period where participants will be asked to avoid consuming foods rich in anthocyanins. After the 28 day intervention period, there will be a 3 week wash out period after which the participant will be asked to then drink the other juice for 28 days. The 500 mL of blood orange juice will contain approximately 50mg of anthocyanins, whereas the standard juice will contain none.

Blood samples will be collected for the preparation of plasma and peripheral blood mononuclear cells (PBMCs) for the analysis of anthocyanin metabolite concentrations, transcriptomics and CVD risk markers. Urine samples will be collected and urinary excretion of anthocyanin metabolites will be quantified. Other measurements will include pulse wave analysis, pulse wave velocity, central blood pressure, waist and hip circumference, blood glucose, glycated haemoglobin (HbA1C) and insulin concentrations, and various measurements using the TANITA machine which include weight, fat mass, muscle mass, fat percentage, fat-free mass, total body water, bone mass, metabolic age, basal metabolic rate, visceral fat rating, and degree of obesity. All measurements and samples will be taken at baseline and post intervention for each phase of the study. This study is part of the EU funded FP7 ATHENA project.

Follow Up Length: 0 month(s); Study Entry : Registration only

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
LDL-cholesterol, measured at baseline and 28 days after ingestion of standard blonde orange juice and blood orange juice

Key secondary outcome(s))
1. Gene expression
2. Markers of CVD (total cholesterol, HDL-cholesterol, nitric oxide, CRP, insulin, glucose, ET-1)

Measured at baseline and 28 days after ingestion of standard blonde orange juice and blood orange juice.

Completion date
31/12/2017

Eligibility

Key inclusion criteria
1. Men and women aged 25-84 years
2. Waist measurement
2.1. Caucasians: Men > 102 cm (40 inches); Women >88 cm (34 inches)
2.2. Asians: Men > 90 cm (35 inches); Women 80 cm (31 inches)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Those unable to give written informed consent
2. Those unwilling to provide GP details
3. Regular prescribed medication that may affect study outcome. This will be assessed on an individual basis-not including statins
4. Over-the-counter (non-prescribed) medication that may affect the study data. This will be assessed on an individual basis.
5. Allergy to the test juice drink or the actual fruit itself
6. Chronic medical conditions requiring active treatment. This will be assessed on an individual basis
7. Those already consuming blood orange juice, unless they are willing to discontinue consumption for 2 weeks prior to starting the study.
8. Diagnosed diabetics;
9. Peri-menopausal women (defined as: when there is a permanent change in menstrual cycle)
10. Women on HRT for less than one year
11. On thyroxine for less than one year
12. Women who are pregnant, have been pregnant within the last 12 months or who are breastfeeding
13. Those taking aspirin (prescribed or self-prescribed)
14. All blood pressure medication
15. Those individuals who happen to be on statins will be excluded if they have been on statins for less than 3 months; or if they are not taking on a daily basis; or those who have recently changed their dosage of statins. This will be assessed on an individual basis
16. Those on regular medication for hypercoagulation and inflammatory conditions e.g. corticosteroids and asthma. The intermittent use of an inhaler will be discussed on an individual

basis
17. Those who have had a cardiovascular event such as stroke, myocardial infarction (heart attack) or trans ischemic attacks in the past and deemed unsuitable for participation in the study. This will be discussed with the medical advisor on an individual basis
18. Peripheral vascular disease including claudication
19. Consumption of fish oil supplements (unless participant is willing to discontinue their use 8 weeks prior to the start of the intervention- all other supplements will be assessed on an individual basis
20. Parallel participation in another research project which has involved dietary intervention and /or sampling of blood
21. Any person related to or living with any member of the study team
22. Participation in another research project which involves blood sampling within the last four months unless the total blood from both studies (including this one) does not exceed 470mL)
23. Those who have donated or intend to donate blood within 16 weeks of the first and last study samples
24. Gastrointestinal disease (excluding hiatus hernia) unless symptomatic or study intervention /procedure is contraindicated
25. Those undergoing any on-going clinical investigations with their GP or hospital clinic.
26. Those who have had throat surgery or neck injury
27. Those with internal medical devices

Screening exclusion criteria:
1. Results of the eligibility screening that indicate or are judged by the HNU medical advisor to be indicative of a health problem which could compromise the well-being of the participant if they participated or could affect the study data.
2. BMI <19.5
3. Weight >180kg (28stones)
4. Fasting total cholesterol > 8.0mmol/L

Date of first enrolment
01/08/2014

Date of final enrolment
01/05/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Food Research
Norwich Research Park
Colney Lane
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NR4 7UA

Sponsor information

Organisation
Institute of Food Research (UK)

ROR
https://ror.org/04td3ys19

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated as part of the current study will be available upon request from paul.kroon@ifr.ac.uk once the results have been published in a high-impact journal.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2018	10/06/2019	Yes	No
HRA research summary			28/06/2023	No	No