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Mechanistic and efficacy studies on a tomato extract with antiplatelet properties

Submission date 15/02/2016	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 16/02/2016	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 28/03/2018	**Condition category** Other	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Several studies have shown that populations who consume a Mediterranean diet enjoy a degree of protection from heart disease. A link to tomato consumption has been suggested, which could be in part due to the anti-blood-clotting (antiplatelet) properties of tomatoes. Based on extensive research carried out by Provexis Natural Products Limited using the branded tomato extract Fruitflow, a heart healthy fruit juice drink was tested in the UK throughout 2006 under the brand name Sirco. Other commonly consumed foods can also have antiplatelet effects, such as fish oils, garlic and cocoa, but when consumed in normal dietary amounts the antiplatelet effects are often small. For example, you would need to consume 3g of fish oil per day for at least several weeks to have an antiplatelet effect. We are interested in combining mild dietary antiplatelets and Fruitflow to increase their antiplatelet effects. However, most dietary antiplatelets are impractical choices for a study as we are not sure how they work or what dose is required, or the quantities which must be consumed are too high. In addition, we would like to focus our study on acute antiplatelet effects, i.e. effects immediately after consumption of a single dose, and we would like to select an antiplatelet which works in a different way to Fruitflow. The range of dietary antiplatelets with such effects is very limited. Therefore to allow us to begin our research into the interactions of Fruitflow with other antiplatelets, we have selected the commonly used over-the-counter drug aspirin at a low dose as our second antiplatelet. Low-dose aspirin is a common part of daily life for many individuals, and its mechanism of action and dosage requirements are all well established and different to that of Fruitflow. Its use is also not associated with side effects in healthy volunteers over a short time. We wish to investigate the effects of repeated intake of Fruitflow along with a daily dose of aspirin. This will ensure that the effects of aspirin and Fruitflow are likely to overlap over the course of the study day. These data will enable us to judge whether the tomato extract has any additional effects on the clotting system of healthy volunteers when taken with a daily dose of aspirin.

Who can participate?
Healthy subjects aged 45 - 75

What does the study involve?
Participants are randomly allocated to take one of two treatments: either aspirin (plus three

placebo [dummy] capsules) taken once per day for seven consecutive days, or an apparently identical placebo capsule set. On day 1, participants provide a blood sample before consuming the first capsule, and the effect of this capsule is assessed after 3 and 5 hours. Participants then depart, taking with them a supply of capsules to be taken once per day for the following seven days. On the morning of day 8, participants return to the study unit and a blood sample is taken to measure the effect of the capsules they had taken for the intervening seven days. The participants then consume 3g of Fruitflow, along with their other capsules. Again, blood samples are taken after 3 and 5 hours, after which the participants are free to leave. All participants undertake this process twice, switching between the aspirin and placebo capsules with a break of 14 days (minimum) in between.

What are the possible benefits and risks of participating?
Participants are healthy volunteers and as such do not benefit directly from involvement in the study. Participants are informed of the reason for the study, and became involved to help with development of a new functional food which might possibly benefit them in the future. Participants are recompensed for lost time and transport costs. Risks associated with the study are related to blood sampling. Participants with particularly thin/thread veins or whose veins are not clearly palpable are excluded from the study. Attempts at blood sampling are limited to four, in order to prevent activation of the clotting system. All blood samples are taken by an experienced nurse phlebotomist, and a closed syringe system is used for the blood collections, minimising risk of blood contact.

Where is the study run from?
University of Aberdeen (UK)

When is the study starting and how long is it expected to run for?
May 2007 to March 2010

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Niamh O'Kennedy

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
08/S0802/196

Study information

Scientific Title
Assessing possible interactions between Fruitflow tomato extract and aspirin in apparently healthy subjects

Study objectives
This study aims to investigate the effect of Fruitflow on platelet aggregation with and without concomitant aspirin (75mg/d) use in apparently healthy volunteers. The hypothesis is that high doses of Fruitflow, in excess of the recommended daily intake, when taken with concomitant daily use of 75mg aspirin, will not produce an inhibitory effect on the haemostatic system that is more than the additive effects of Fruitflow and aspirin alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North of Scotland Research Ethics Committee (NOSRES), 14/01/2009, ref: 08/S0802/196

Study design
Single-centre intervention study following a randomised double-blinded placebo-controlled cross over design with two treatments

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Examination of platelet function and response to potentially beneficial dietary supplements in healthy subjects

Interventions
The study involved two base treatments, either 75mg aspirin (plus three placebo capsules) taken once per day for seven consecutive days, or an apparently identical control capsule set. On day 1, a baseline blood sample was taken before consuming the first intervention supplement, and the acute effect of this supplement was assessed at t=3 and t=5 hours. Subjects then departed, taking with them a supply of capsules to be taken once per day for the following seven days. On the morning of day 8, subjects returned to the study unit, and a blood sample was taken to measure the effect of the supplements they had taken for the intervening seven days. The subjects then consumed 3g of the tomato extract, concomitantly with their seven-day supplement. Again, blood samples were taken at t=3 and t=5 hours, after which the subjects finished their intervention and were free to leave. All subjects undertook this intervention pattern twice, crossing over the aspirin and placebo supplements with a washout period of 14 days (minimum) in between. The minimum duration of the set of interventions was 30 days.

Intervention Type
Supplement

Primary outcome measure
Changes in platelet function in response to agonist, changes in platelet thromboxane generation and changes in PFA-100 closure time (time to form a primary clot) at t3 hours after supplementation

Secondary outcome measures
1. Changes in platelet-related parameters at t5 hours after supplementation
2. Changes in plasma clotting times at t3 and t5 hours after supplementation

Overall study start date
01/05/2007

Completion date
03/03/2010

Eligibility

Key inclusion criteria
1. Healthy subjects
2. Male and female
3. 45 - 75 years of age
4. Normal platelet function

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
46

Key exclusion criteria
1. Low platelet number in whole blood (< 170 x 109/ L)
2. Hematocrit below 40% for males or below 35% for females
3. Haemoglobin below 120 g/L for males or below 110 g/L for females
4. Prothrombin time (PT) values outside the normal range of approximately 10 – 16 s
5. BMI below 18 or above 38 kg/m2
6. Overt vascular or haematological disease, hypertension or infection
7. Clinically significant chronic illnesses
8. Known susceptibility to GI irritation, e.g. history of gastric ulcers
9. Consumption of aspirin, corticosteroids, other (non steroidal) anti–inflammatory drugs or other drugs or herbal medicines known to alter platelet function or the haemostatic system in general (without a minimum washout period of two weeks)
10. Consumption of evening primrose oil or fish oil supplements (without a minimum washout period of one month)
11. Consumption of a contraceptive pill or hormone replacement therapy
12. Pregnancy
13. Intolerance/allergy to aspirin
14. Allergy to tomatoes
15. Unsuitable veins for blood sampling and/or cannulation
16. Donation of one pint of blood or more for transfusion purposes in the past month before entry into the study
17. Smoking

Date of first enrolment
01/05/2007

Date of final enrolment
01/12/2007

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
The University of Aberdeen
Rowett Institute of Nutrition and Health
Greenburn Road

Bucksburn
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AB21 9SB

Sponsor information

Organisation
Provexis plc (UK)

Sponsor details
Prospect House
58 Queens Road
Reading
United Kingdom
RG1 4RP

Sponsor type
Industry

ROR
https://ror.org/046pkq184

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
The study is intended for publication in a peer reviewed journal. A full description of the protocol, results and conclusions of the study will be published. The exact date of publication is not yet known.

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2017		Yes	No