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Effects of Annurca apple polyphenols on cholesterol metabolism in healthy subjects

Submission date	Recruitment status	[X] Prospectively registered
17/11/2015	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
18/11/2015	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
18/11/2015	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Atherogenic dyslipidemia, is condition where there is a disease causing (pathological) imbalance of circulating lipoproteins (fats in the blood) such as LDL (low-density lipoprotein), VLDL (very low-density lipoprotein), or IDL (intermediate-density lipoprotein) over others suvh as HDL (high-density lipoprotein). It is a major risk factor for the development of cardiovascular disease, such as coronary heart disease and stroke (CVD). Previous research suggests that high levels of HDL-C (high-density lipoprotein cholesterol) lowers the risk of CVD. Until now, treatments to prevent CVD have focused on lowering the level of LDL in the blood, but new therapies to increase HDL levels are now emerging to treat the imbalance seen in atherogenic dyslipidemia. As a result, there is now a need to find novel HDL-raising agents (e.g. drugs). Some published human studies have investigated the TC (total cholesterol)-lowering effects of polyphenols (micronutrients which may help prevent diseases such as CVD and cancer) from apples or apple products. Until now, the effects are rather low and not enough to be effective for CVD prevention. However, different varieties of apple may contain very different amounts of polyphenols. The Annurca apple, for example, has been shown to have a higher polyphenolic concentration that some of the more common commercial apple varieties, including Red Delicious, Pink Lady, Granny Smith, Fuji and Golden Delicious. It is also known to be the apple that works best at reducing the amount of cholesterol taken up into body cells, increase the activity of proteins called LDL-C receptors (these bind LDL which is then taken into body cells to be broken down into cholesterol which is then either used by the body or removed) and increasing the amount of Apolipoprotein A1, a major protein found in HDL. The aim of this study is to look at the effects of the Annurca apple and its polyphenolic extract on plasma cholesterol (blood cholesterol) in healthy people with slightly raised blood cholesterol and compare them with more conventional apple cultivars.

Who can participate?
Adults aged 18-83, white and with slightly high blood cholesterol levels.

What does the study involve?
The participants are randomly allocated to one of six groups. All participants in all groups start with a "placebo" period of four weeks (referred to as weeks -4 to 0) where they just carry on as usual, after which they receive a specific treatment. Those in group 1 are given two Annurca apples to eat a day for one month. Those in group 2 are given one Red Delicious apple to eat a

day for one month. Those in group 3 are given one Fuji apple to eat a day for one month. Those in group 4 are given one Granny Smith apple to eat a day for one month. Those in group 5 are given one Golden Delicious apple to eat a day for one month. Those in group 6 are given two gastric-resistant capsules containing Annurca apple polyphenolic extract, at 800 mg/day, for one month. After one month, all participants go though another "placebo" period of 4 weeks before being randomly assigned to one of the other treatment groups for a further 4 weeks. All participants go though two treatment periods (for example, being randomly allocated to the Annurca apple group, followed by going though the placebo period, followed by being randomly assigned to the Granny Smith group). Fasting blood samples (that is, blood samples that are taken after 12 hours of not eating) are collected from each participant at the beginning of the "placebo" period (week -4), at the beginning of the study and then every four weeks until the end of the study. These samples are analysed to test for TC, LDL-C and HDL-C levels and also liver and kidney function.

What are the possible benefits and risks of participating?
Participants may benefit from a healthier balance of the lipoproteins in their blood. No side effects are expected.

Where is the study run from?
The blood samples are collected by the Samnium Medical Cooperative (Benevento, Italy) and analysed at the Department of Pharmacy, University of Naples “Federico II” (Naples, Italy).

When is the study starting and how long is it expected to run for?
November 2015 to January 2016.

Who is funding the study?
Hospital AO Rummo (Italy)

Who is the main contact
Professor Gian Carlo Tenore
giancarlo.tenore@unina.it

Contact information

Type(s)
Scientific

Contact name
Prof Gian Carlo Tenore

ORCID ID
http://orcid.org/0000-0002-0251-9936

Contact details
Via Domenico Montesano 49
Naples
Italy
80131
+39081678610
giancarlo.tenore@unina.it

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
18.07.2015 14303

Study information

Scientific Title
Evaluation of Annurca apple polyphenols on cholesterol metabolism in mildly hypercholesterolemic healthy subjects: a monocentric, randomised, cross-over, placebo-controlled 4 weeks study

Acronym
ANNURCHOLEST

Study objectives
Apple contains several phenolic compounds, which are known for its health benefits. Since it has been demonstrated that Annurca apple is characterised by a higher concentration of these polyphenolic compounds than other more conventional apple cultivars,

Aim 1: Compare the effects of apple consumption on the plasma levels of TC, LDL-C, HDL-C, and blood pressure, in the subjects.

Aim 2: Compare the effects of Annurca apple polyphenolic extract administration on the plasma levels of TC, LDL-C, HDL-C, and blood pressure, in the subjects

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hospital AO Rummo (Benevento, Italy), 18.07.2015, ref: 14303

Study design
Intervention trial, parallel, randomized, open and controlled

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Metabolic Syndrome (MeTS)

Interventions
The study is a monocentric, randomised, cross-over, placebo-controlled 4 weeks study on 500 mildly hypercholesterolemic healthy volunteers, 284 men and 266 women.

The subjects enrolled in this study have the following values of serum cholesterol parameters at baseline (week 0): TC, 200-260 mg/dL; HDL-C, 31-45 mg/dL; LDL-C, 189-206 mg/dL. The subjects are asked to keep their dietary habits unchanged throughout the entire study.

After going though a 4 week "placebo" period, patients are randomly divided into six groups. Four groups are assigned to consume one apple/day among the following: Red Delicious, Granny Smith, Fuji, Golden Delicious. The fifth group is asked to consume two Annurca apples/day, since the weight of this cultivar is on average the half of the commercial ones considered in this study. The sixth group is given two gastric-resistant capsules containing Annurca apple polyphenolic extract, accounting for 800 mg/day. After one month, all participants go though another "placebo" period of 4 weeks before being randomly assigned to one of the other treatment groups for a further 4 weeks.

Blood samples of volunteers are collected after 12 h of fasting at week -4, 0, and 4 and are analysed to monitor the lipid profile (TC, LDL-C, and HDL-C) and hepatic and renal function.

Intervention Type

Primary outcome measure
1. Plasma TC, HDL-C, and LDL-C levels are determined at the beginning (week -4) of the trial, after the placebo period (week 0), and at the end of the interventional study (week 4). Analyses are performed on a Diacron International Free Carpe Diem spectrophotometer (Grosseto, Italy), by using commercially available kits from Diacron International.
2. Higher positive effects on the balance of plasma cholesterol parameters, as regards the apple interventional study, are expected in the subjects belonging to group ANN in comparison to the others groups.

All variables (primary and secondary outcomes) will be measured at baseline and after each intervention period.

Secondary outcome measures
1. At the beginning and end of each intervention period a medical assessment will be performed which included: clinical history, dietary evaluation, anthropometric measures, clinical blood pressure and 24-hour ambulatory blood pressure, blood analysis (TC, HDL-C, LDL-C, AST, ALT, γ-GTP, ALP, LDH, Albumin, Total bilirubin, Creatinine).
2. A 7-day food record validated nutritional questionnaire will be used at the beginning and end of the intervention to assess nutrient intake and to monitor the dietary habits.

Overall study start date
23/11/2015

Completion date
30/01/2016

Eligibility

Key inclusion criteria
Men and women between 18-83 years of age, of white race, with the following range values of serum cholesterol parameters at baseline (week 0):
1. TC, 200-260 mg/dL
2. HDL-C, 31-45 mg/dL
3. LDL-C, 190-205 mg/dL.
4. Body mass index (BMI) between 18 and 30 kg/m2

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
83 Years

Sex
Both

Target number of participants
500

Key exclusion criteria
Healthy adults (males and females) with:
1. Smoking
2. Obesity (BMI >30 kg/m2)
3. Diabetes
4. Hepatic disease
5. Renal disease
6. Heart disease
7. Family history of chronic diseases
8. Drug therapy or supplement intake for hypercholesterolemia
9. Drug therapy or supplement intake containing apple polyphenols
10. Heavy physical exercise (>10 h/week)
11. Pregnant women, women suspected of being pregnant, women who hoped to become pregnant, breastfeeding

12. Birch pollen allergy
13. Use of vitamin/mineral supplements 2 weeks prior to entry into the study
14. Donation of blood less than 3 months before the study

Date of first enrolment
23/11/2015

Date of final enrolment
27/11/2015

Locations

Countries of recruitment
Italy

Study participating centre
Samnium Medical Cooperative
Viale C.Colombo, 18
Benevento
Italy
82037

Study participating centre
Department of Pharmacy, University of Naples “Federico II”
Via Domenico Montesano 49
Naples
Italy
80131

Sponsor information

Organisation
Hospital AO Rummo

Sponsor details
Via dell’Angelo, 1
Benevento
Italy
82100
+390824.940424
dr.domenicocaruso@gmail.com

Sponsor type

Hospital/treatment centre

ROR
https://ror.org/00cmfmh53

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Samnium Medical Cooperative (Italy)

Funder Name
University of Naples “Federico II” (Naples, Italy).

Results and Publications

Publication and dissemination plan

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available