

# Effects of Annurca apple polyphenols on cholesterol metabolism in healthy subjects

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 18/11/2015	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 18/11/2015	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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 such 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 than 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 through 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 through two treatment periods (for example, being randomly allocated to the Annurca apple group, followed by going through 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

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## Contact information

### Type(s)

Scientific

### Contact name

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# Additional identifiers

## Protocol serial number

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

## Study type(s)

Prevention

## 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 through 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 through 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(s)**

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.

### **Key secondary outcome(s)**

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,  $\gamma$ -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.

### **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/m<sup>2</sup>

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

83 years

**Sex**

All

**Key exclusion criteria**

Healthy adults (males and females) with:

1. Smoking
2. Obesity (BMI >30 kg/m<sup>2</sup>)
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

### **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**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not expected to be made available