ISRCTN37548161 https://doi.org/10.1186/ISRCTN37548161

POlyphenol CardioMetabolic Outcomes Study: The effects of green tea and coffee extracts on glucose metabolism and cardiovascular function in overweight and obese women with Polycystic Ovary Syndrome (PCOS) and insulin resistance

Submission date
23/02/2014

Recruitment status
No longer recruiting

Registration date
16/04/2014

Overall study status
Completed

Last Edited
25/11/2019

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Polycystic Ovary Syndrome (PCOS) is characterised by insulin resistance (body tissues have a reduced response to the effect of insulin). PCOS is made worse by obesity and by increased insulin levels. A reduction in insulin sensitivity (ability of body tissues to respond to action of insulin) and a decrease in the production of nitric oxide (released from the lining of the blood vessels, which causes them to relax allowing blood to flow normally) expose women with this condition to an increased risk for diabetes and heart disease. Substances present in green tea and coffee are called polyphenols. They appear to have beneficial effects on the regulation of blood glucose and on risk factors for heart disease (e.g. elevated blood pressure). However there is not enough evidence from previous research. This study evaluates the potential positive effect of green tea and coffee polyphenols on insulin sensitivity, nitric oxide production and risk factors for heart disease in overweight and obese women with PCOS and insulin resistance.

Who participated?
Pre-menopausal, overweight or obese women with PCOS and insulin resistance who are 16-45 years of age

What did the study involve?
All participants take placebo (dummy) tablets for 8 weeks and green tea and coffee polyphenol tablets for the following 8 weeks. Height, weight, waist circumference and body fat percentage, glucose control, heart function measurements and other related parameters are tested before and after taking thel tablets. In addition diet and physical activity level are assessed and safety and compliance checks are conducted at these times. Consumption of foods containing polyphenols (e.g. fruits, vegetables, cocoa products, etc.) is only restricted during the 3 days before each main study visit. The effect of the polyphenol tablets is compared with that of the dummy treatment.

What were the possible benefits and risks of participating?
Participants benefit from been screened for diabetes, high cholesterol, triglycerides and high blood pressure. They are given the option to know their weight, body mass index (BMI) and body fat percentage throughout the study. Participants also learn about the overall results of the study (mainly in relation to glucose control and heart function). Knowledge gained from this study could help improve the understanding of the potential use of polyphenols in protecting against the development of diabetes and heart disease. The main risks associated with participation in this study are from blood taking which may cause discomfort and minor bruising in some instances, and side effects associated with the intake of the polyphenol tablets (e.g. mild stomach ache). No side effects are associated with taking the placebo treatment. The body composition measurement involves negligible exposure to ionizing radiation (equivalent to about 9 hours natural background radiation in the UK). The tests for insulin sensitivity and nitric oxide production involve the use of stable isotopes (naturally occurring molecules) which do not have any risk for human health.

Where was the study run from?
Medical Research Council (MRC) - Human Nutrition Research (HNR) (UK)

When did the study start and finish?
April 2012 to November 2013

Who is funding the study?
Medical Research Council (MRC) - Human Nutrition Research (HNR) (UK) (UK)

Who is the main contact?
Mrs Virginia Tomatis

Contact information

Type(s)
Scientific

Contact name
Mrs Virginia Tomatis

Contact details
MRC Human Nutrition Research
Elsie Widdowson Laboratory
120 Fulbourn Road
Cambridge
United Kingdom
CB1 9NL

Additional identifiers

Protocol serial number
6420

Study information

Scientific Title
The effects of green tea and coffee polyphenols on insulin sensitivity and secretion and cardiovascular function in overweight and obese women with Polycystic Ovary Syndrome (PCOS) and insulin resistance

Acronym
POCMOS

Study objectives
Primary hypotheses:
1. Combined supplementation with green tea and coffee polyphenols will result in an increase in insulin sensitivity and improvement in insulin secretion in overweight and obese women with Polycystic Ovary Syndrome (PCOS) and insulin resistance.
2. Combined supplementation with green tea and coffee polyphenols will result in an increase in nitric oxide production.

Secondary hypotheses:
1.. Combined supplementation with green tea and coffee polyphenols will result in an improvement in vascular/endothelial function.
2. Insulin sensitivity and nitric oxide will be positively associated and they will be positively correlated with improved vascular/endothelial function.
3. Combined supplementation with green tea and coffee polyphenols will produce a reduction in oxidative stress and inflammatory biomarkers.
4. Combined supplementation with green tea and coffee polyphenols will result in a greater increase in insulin sensitivity and nitric oxide production (synergistic effect) compared with the results from previous studies investigating the effects of each substance alone in similar populations.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridge South Research Ethics Committee, 02/03/2012, ref: 11/EE/0465

Study design
Single-blind placebo-controlled unilateral cross-over study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Polycystic Ovary Syndrome (PCOS), overweight/obesity and insulin resistance

Interventions
The study consisted of two intervention treatments:
1. Placebo treatment - placebo tablets
2. Active treatment (polyphenol supplements) - Green Tea extract (GTE) tablets (containing green tea catechins, GTC) and Verdesse® tablets (containing chlorogenic acids, CGA)

Green Tea extract (GTE) tablets were purchased from Healthspan (St Peter Port, UK). The total amount of GTC and CGA consumed by participants per day during the intervention period was approximately1938 mg and 600 mg respectively (approximately equivalent amount of GTC and CGA to that of drinking 8 to 13 cups of green tea and 2 to 9 cups of coffee per day). Participants took placebo tablets for eight weeks, followed by eight weeks of GTC and CGA tablets. GTC tablets (and their corresponding placebo tablets) were taken 30-60 minutes before breakfast, lunch and dinner. CGA tablets (and their corresponding placebo tablets) were taken immediately after breakfast, lunch and dinner).

Intervention Type
Supplement

Primary outcome(s)
Insulin sensitivity and secretion were measured at baseline (week 0), post-placebo (week 8) and post-intervention (week 16) time points via the Oral Dose Intravenous Labelled Glucose Experiment (ODILE) protocol. The ODILE protocol is similar to the Oral Glucose Tolerance Test (OGTT), but it is modified by the addition of an intravenous dose of [1]-13C-glucose (labelled glucose) administered 45 minutes after the oral glucose dose was consumed (40 blood samples are taken over a 4-hour and 45 minute period). Gas chromatography/combustion/isotope ratio mass spectrometry (GC/C/IRMS) is used for isotopic composition and the results are interpreted using a stable-label two compartment minimal model (2CMM). This mathematical modelling allows for the determination of glucose effectiveness and insulin sensitivity parameters. Insulin and C-peptide data obtained from the same protocol were also modelled to obtain information about insulin secretion.

Key secondary outcome(s))
1. Nitric oxide production was also measured at baseline (week 0), post-placebo (week 8) and post-intervention (week 16) using the Oral Nitrate Test (ONT) protocol, which is based on the physiological characteristics of the entero-salivary circulation of plasma nitrate and involves the consumption of a very low nitrate meal, followed by the collection of six saliva samples over a 2-day period. Isotopic composition is measured using GC/MS. The protocol measures the disappearance of an oral dose of Na15NO3 (labelled sodium nitrate) in saliva samples. The isotopic decay is defined by an exponential function for a single compartment. Data are expressed using a semi-logarithmic plot and the slope and intercept of the regression line are utilised to calculate the NO production rate.
2. Vascular/endothelial function measurements were measured at the same time points as stated above; except for blood pressure which was also measured at 2 intermediate study visits (weeks 4 and 12). The measurements consisted of carotid intima media thickness (cIMT), pulse wave velocity (PWV) and blood pressure.

Completion date
27/11/2013

Eligibility

Key inclusion criteria
1. Otherwise healthy
2. Pre-menopausal, overweight or obese women (BMI ≥ 25 kg/m2)
3. Aged16-45 years
4. With PCOS and insulin resistance (fasting insulin ≥ 50 pmol/L)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Total final enrolment
12

Key exclusion criteria
1. Smoking
2. History of substance abuse or alcohol consumption >14 units per week
3. Allergy or intolerance to the study supplements and/or foods
4. Professional athletes or those with self-reported high physical activity
5. Chronic, acute or active metabolic (including type 1 and type 2 diabetes mellitus) and inflammatory conditions, haematological disorders, or any other systemic illness of renal, hepatic or gastrointestinal origin
6. Active cancer or diagnosis of malignancy within the last five years
7. Major surgical operations interfering with the study outcomes within three months of screening
8. Medical treatment with the following agents: weight reduction medicines, insulin sensitizers, hormonal therapy, antihypertensive medicines, anti-dyslipidaemic agents, nitrate-derived agents, psychiatric drugs (only excluded if dose had been started/changed in the previous six months) or any other medication known to affect glucose/insulin metabolism, vascular /endothelial function, gastrointestinal system or central nervous system
9. Weight change > 10% over the last six months
10. Endocrine disorders such as adrenal hyperplasia, hyperprolactinaemia, Cushings syndrome, androgenic tumours, late onset of 21-hydroxylase deficiency, abnormal thyroid function or any other ovarian, adrenal or pituitary disorder not associated with PCOS
11. Pregnant, lactating, contemplating pregnancy or undergoing treatment to achieve pregnancy
12. Regular consumption of micronutrient and/or herbal and/or polyphenol supplements known to have an impact on insulin sensitivity/secretion and/or vascular/endothelial function

Date of first enrolment
17/04/2012

Date of final enrolment
01/07/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
MRC Human Nutrition Research
Cambridge
United Kingdom
CB1 9NL

Sponsor information

Organisation
Medical Research Council - Human Nutrition Research (UK)

ROR
https://ror.org/050pqs331

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) - Human Nutrition Research (HNR) (UK), programme number 5PT60

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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	results presented at Experimental Biology conference	01/04/2015	25/11/2019	No	No