Dietary polyphenols as modulators of lipid oxidation and mitochondrial function in overweight volunteers

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Driven by the hypothesis that combination of dietary polyphenols, with distinct mechanisms of action, may improve cellular energy and fatty acid metabolism, preventing thereby the development of the metabolic syndrome and diabetes, the following...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON38206

Source
ToetsingOnline

Brief title
Polyphenols and fat oxidation

Condition

- Lipid metabolism disorders

Synonym
impaired fat oxidation, overweight

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Alpro Foundation

Intervention

Keyword: fat oxidation, mitochondrial function, overweight, polyphenols

Outcome measures

Primary outcome

The primary study parameter is the difference in postprandial fat oxidation

after the 3 polyphenol conditions

Secondary outcome

As secondary endpoints, differences in the systemic and local tissue lipolysis,

mitochondrial function, oxidative stress, insulin sensitivity and body

composition between the various polyphenol supplements are examined.

Study description

Background summary

There is an urgent need for additional preventive strategies against obesity, diabetes and the metabolic syndrome since the increasing prevalence of these diseases is one of the major health care problems in both developed as well as developing countries. Dietary polyphenols may have the potential to improve lipid oxidation and mitochondrial function and may consequently contribute to the prevention of diabetes and the metabolic syndrome. So far, no studies have addressed the additive or possibly synergistic effects of combinations of specific polyphenols with partly distinct mechanisms of action on fat oxidation and metabolic profile in overweight subjects.

Study objective

Driven by the hypothesis that combination of dietary polyphenols, with distinct mechanisms of action, may improve cellular energy and fatty acid metabolism, preventing thereby the development of the metabolic syndrome and diabetes, the following objectives will be addressed:

(1) to test short term (3 day) effects of combinations of polyphenols (supplements of EGCG either in combination with resveratrol or with resveratrol and soy isoflavones) to affect systemic lipolysis and fat oxidation during

overnight fasted conditions and after ingestion of a high fat meal in overweight subjects;
(2) to perform a randomized controlled intervention study with the most promising combination of dietary polyphenols, investigating its effect on fat oxidation, mitochondrial function and insulin sensitivity in overweight subjects over a 12 wk period.

Study design

Study 1
A double blind placebo controlled cross over design with 3 treatments will be used. Treatment duration will be 3 days with a 7 day wash-out period in between. Treatments will be (1) the combination of of EGCG (282 mg daily) and resveratrol (200 mg daily), (2) these 2 polyphenols combined with soy isoflavones (48 mg genistein daily) or (3) placebo. Supplements will be taken twice a day at breakfast and dinner. At day 3, 13 and 23 circulating metabolite concentrations, catecholamines, oxidative stress markers and fat oxidation will be determined in plasma and urine samples during overnight fasted conditions and after a high fat test load. On the end of the testday an adipose tissue biopsy will be taken.

Study 2
Duration of the study will be 12 weeks. A double blind parallel design will be used. Overweight subjects will be randomized to polyphenol supplementation or placebo with stratification for age and sex. Before and after intervention, at one day, measurements on fat oxidation during fasting and after a high fat mixed meal will take place and, at a second day, insulin sensitivity will determined. Body composition will be determined before and after intervention by means of DEXA scanning. On a separate day, adipose tissue and muscle biopsies will be taken and depending on the outcome further molecular characterization of pathways of lipolysis, fat oxidation, mitochondrial function and insulin sensitivity will be performed. Faeces will be collected on the biopsy day. In 10 subjects of each group, local adipose tissue lipolysis will be determined by microdialysis during the high fat meal.

Intervention

3 different dietary polyphenol conditions:

A. EGCG (282mg daily) + resveratrol (200mg daily)
B. EGCG (282mg daily) + resveratrol (200mg daily) + soy isoflavones (48mg genistein daily)
C. Placebo

Study burden and risks

Results obtained from the study provide insight on the possible positive effects of various combinations of polyphenols on postprandial fat oxidation. A higher postprandial fat oxidation could lead to less accumulation of lipid in the fat and muscles tissue causing improvement in insulin sensitivity and metabolic profile on the long-term.
The study carries minor to no risks for the subjects. The only burden comes from taken blood samples, placement of the microdialysis probes and taking skeletal muscle and adipose tissue biopsies. These burdens will be kept as small as possible.

For study 1 the subject visits the university 4 times (screening + 3 long testdays; total duration of 23 days with a wash-ot of 7 days in between). During the long testdays a total of 603 ml blood will be taken and the subject needs to wear the ventilated hood system to measure fat oxidation. At the end of the testday testday an adipose tissue biopsy will be taken.
For study 2 the subject visits the university 3 times before and 3 times after the 12 week intervention for. During the testdays a total of 350 ml blood will be taken and the subject needs to wear the ventilated hood system to measure fat oxidation, fat and muscle biopsies are taken, faeces be collected and microdialysis probes are inserted (optional).

Contacts

Public
Universiteit Maastricht

PO Box 616
6200 MD Maastricht
NL
Scientific
Universiteit Maastricht

PO Box 616
6200 MD Maastricht
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Overweight men and women (BMI>=25kg/m2- 34.9kg/m2),
- Aged 20-35 and 35-50 years
- Caucasian
- Normal fasting glucose (< 6.1 mmol/L)
- Normal blood pressure (systolic blood pressure 100-140 mmHg, diastolic blood pressure 60-90 mmHg)
- Weight stable in last 3 months (± 2kg).

Exclusion criteria

- Women lactating, pregnant or (post) menopausal
- Regular smokers
- People with intensive fitness training, eg. athletes (>= 3 per week >= 1 hour training)
- Habitual consumption of green tea (more than 1 cup per day) or products containing green tea extract
- Total caffeine consumption > 300 mg/day (1 can of cola or 2 cups of regular coffee or 2 cups of black tea or 1 cup of coffee and 1 cup of black tea or other combinations)
- Alcohol intake >20 g/day (2 glasses of beer or wine)
- Any dietary vitamins or dietary supplements
- Diabetes mellitus (defined as FPG >= 7.0 mmol/l and/or 2hPG >= 11.1 mmol/l)
- Serious pulmonary, cardiovascular, hepatic or renal disease
- History of cardiovascular disease
- All other relevant medical disorders that potentially interfere with this trial (e.g. history of gastro-intestinal, liver or thyroid disorders)
- Current use of medication interfering with study intervention or interfering with study endpoints/hypotheses (e.g. medication containing caffeine like analgesics, anorectics and analeptics)
- Not to be able to understand the study information
- Subjects on a special diet or vegetarian
- Blood donation 2 months prior to the study and during the study
- Participation in other studies
- Drug use
- Use of anti-coagulant medication

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-03-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-04-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-05-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	22-05-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01302639
CCMO	NL31421.068.10