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Colonic propionate, appetite and glucose homeostasis

Submission date	Recruitment status
26/09/2014	No longer recruiting
Registration date	**Overall study status**
26/09/2014	Completed
Last Edited	**Condition category**
10/05/2021	Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Dietary fibre is anything that we eat that our body is unable to breakdown or digest. However, in our guts we have trillions of bacteria, collectively known as the gut microbiota, that are able to 'eat' the fibre in our food. This process allows the gut microbiota to produce energy to survive and grow. The main 'end-products' of this process are called short chain fatty acids (SCFA) and scientific work is continuing to link these SCFA with improvements in human health. An increased production of SCFA in the gut has been linked to reductions in body weight and improvements in blood glucose levels. We have developed a novel dietary supplement called a propionate-ester that increases the amounts of a SCFA called propionate produced in the gut. Our previous work has shown the feeding the propionate-ester to overweight and obese humans prevented further gains in body weight and reduced the amount of fat in the liver. The current project has two separate studies. The aim of study one is to investigate the effect of the propionate-ester on blood glucose levels in overweight adults. The aim of study two is to look at the effect of the propionate-ester on the amounts of liver fat in individuals with a previous diagnosis of non-alcoholic fatty liver disease (a condition where individuals have higher levels of liver fat).

Who can participate?
Adults aged 18 to 65 who have a BMI between 25-41 kg/m2.

What does the study involve?
If you participate in Study 1, you will be asked to complete three supplementation periods lasting 42 days. During each supplementation period you will be provided with a different dietary fibre to add to your diet. The dietary fibres are all in a powder form that mixes easily into your normal food and drink. At the end of each 42 day period you will be asked to attend our Clinical Research Facility where we will collect blood samples to look at the effects of each dietary fibre on your blood glucose levels. If you participate in Study 2, you will be asked to complete a single 42 day supplementation period. You will be provided with a dietary fibre to mix into your normal diet. Before and at the end of the 42 day period you will be asked to attend our Clinical Research Facility where we will conduct a liver scan to look at the effects of the dietary fibre on liver fat levels.

What are the possible benefits and risks of participating?
There are no direct benefits or risks of taking part in either study.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
February 2014 to July 2017

Who is funding the study?
Biotechnology and Biological Sciences Research Council (BBSRC) (UK)

Who is the main contact?
Dr Edward Chambers (Scientific)
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16734

Study information

Scientific Title
Effect of increased propionate in the colon on appetite and glucose homeostasis

Study objectives

Increased intake of dietary fibre has been associated with reduced appetite and weight loss. In particular, evidence suggests that the fermentable component of dietary fibre is critical in mediating these satiating effects. The short chain fatty acids (SCFAs) produced by microbial fermentation of dietary fibre in the colon have been shown to stimulate the release of appetite suppressing hormones peptide YY (PYY) and glucagon like peptide-1 (GLP-1). Increasing colonic SCFA levels is therefore an attractive target for appetite modulation. To overcome the unpalatably high levels of fermentable dietary fibre needed to significantly increase colonic SCFA levels, we have developed a novel delivery system targeting the release of gram quantities of the SCFA propionate in the human colon. A propionate ester has been produced whereby propionate is chemically bound by an ester bond to inulin, a natural dietary fibre composed mainly of fructose. The majority of propionate bound to inulin should only be released when the inulin polymer is fermented by the colonic microbiota, thus providing targeted colonic delivery. Our previous studies (Effect of Fibre Products on Appetite and Weight; REC Reference: 08 /H0707/99) have found that acute ingestion of propionate ester increases plasma PYY and GLP-1 concentrations and reduces food intake. Furthermore, long-term (24 weeks) ingestion of propionate ester significantly reduced body weight gain and the development of abdominal adipose tissue, major risk factors in the development of insulin resistance and diabetes. The current protocol comprises two follow-on studies which have the following aims:

1. Confirm the appetite suppressing effects of propionate ester when incorporated into a food product.
2. Assess the effects of propionate ester on glucose and lipid metabolism.
Added 24/01/2018:
3. Investigate the impact of propionate ester on hepatic steatosis in adults with non-alcoholic fatty liver disease (NAFLD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Brent, 19/05/2014, ref: 14/LO/0645

Study design
Randomised; Interventional; Design type: Not specified

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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
Topic: Primary Care, Metabolic and endocrine disorders; Subtopic: Metabolic and Endocrine (all Subtopics), Metabolic and endocrine disorders; Disease: Metabolic & Endocrine (not diabetes), All Diseases

Interventions
Study 1: Cellulose, Control; Inulin, Control; Inulin-propionate ester, Inulin-propionate ester; Study Entry : Single Randomisation only

Added 24/01/2018:
Study 2: Inulin, Control; Inulin-propionate ester, Inulin-propionate ester; Study Entry : Single Randomisation only

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Study 1: Glucose homeostasis; Timepoint(s): End of each 6 week intervention

Added 24/01/2018:
Study 2: Intrahepatocellular lipid content

Secondary outcome measures
Study 1: Body composition; Timepoint(s): End of each 6 week intervention

Overall study start date
01/02/2014

Completion date
01/07/2017

Eligibility

Key inclusion criteria
Study 1:
1. Healthy volunteers aged 18-65
2. Male or female
3. Body mass index (weight in kg divided by height in metre squared) of 25-40 kg/m2

Added 24/01/2018:
Study 2:
1. Male or female aged 18-65 years
2. Body mass index (weight in kg divided by height in metre squared) of BMI of 20-40 kg/m2
3. Histological confirmation of NAFLD in previous 5 years.
4. Controlled blood glucose levels (HbA1c <48 mmol/mol)

Participant type(s)

Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
Planned Sample Size: 40; UK Sample Size: 40

Total final enrolment
12

Key exclusion criteria
Study 1 and Study 2:
1. Weight change of more than 3kg in the preceding 3 months
2. Current smokers
3. Substance abuse
4. Excess alcohol intake
5. Pregnancy
6. Diabetes
7. Cardiovascular disease
8. Cancer
9. Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
10. Kidney disease
11. Liver disease
12. Pancreatitis
13. Use of medications including: antiinflammatory drugs or steroids, androgens, phenytoin, erythromycin or thyroid hormones

Study 2 has the additional exclusion criteria:
14. Metallic or magnetic implants such as pacemakers
15. Claustrophobia

Date of first enrolment
13/08/2014

Date of final enrolment
03/03/2016

Locations

Countries of recruitment

England

United Kingdom

Study participating centre
Imperial College London
London
United Kingdom
W12 0NN

Sponsor information

Organisation
Imperial College London (UK)

Sponsor details
Joint Research Compliance Office
Charing Cross Hospital
Fulham Palace Road
London
England
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W6 8RF

Sponsor type
University/education

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Sciences Research Council (BBSRC); Grant Codes: BB/L004259/1

Alternative Name(s)
UKRI - Biotechnology And Biological Sciences Research Council, BBSRC UK, BBSRC

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal. Intention to publish in 2018.

Intention to publish date
01/09/2016

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. The anonymised datasets will be provided as supplementary material in planned publications.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/08/2019	10/05/2021	Yes	No
HRA research summary			28/06/2023	No	No