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Investigating how infusing nutrients into the gut affects gut hormones and appetite

Submission date 28/02/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 05/03/2025	**Overall study status** Ongoing	
Last Edited 05/03/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Obesity rates are rising worldwide, creating an urgent need for safe and effective treatments. Gastrointestinal (GI) hormone-based drugs are emerging as new therapies. The gut contains specialized cells known as enteroendocrine cells (EECs) that release different hormones after meal ingestion. For example, K cells and I cells in the stomach and upper intestines release gastric inhibitory polypeptide (GIP) and cholecystokinin (CCK), respectively, while L cells further down the intestine produce oxyntomodulin (OXM), glucagon-like peptide 1 (GLP-1), and peptide YY (PYY). These hormones send signals to the brain, informing it about the body's energy and nutrient levels, which help regulate food intake. When food is consumed, it is broken down into small molecules (nutrients) that can interact with these hormone-producing cells in the gut. Previous research has shown that the structure of plant foods, such as chickpeas with intact cell walls versus broken cells, can affect which nutrients are present in the gut and how the gut responds. However, it is not yet known which nutrients specifically trigger the production of these hormones and increase feelings of fullness, or where in the gut these signals originate. To explore this, this study will directly infuse nutrients related to chickpea digestion into specific parts of the gut and monitor hormone responses over three hours. By studying these responses, the aim is to identify the key areas of the gut and the nutrients that drive feelings of fullness when digesting legumes. This information could help design plant-based foods that make people feel fuller for longer, supporting weight loss and combating obesity.

Who can participate?
Healthy adult male and female volunteers aged 18 – 65 years old with a BMI of 18 – 30 kg/m²

What does the study involve?
15 healthy participants will be recruited from the healthy volunteer database. They will attend a screening and a 3-day inpatient study visit at the NIHR Imperial Clinical Research Facility.

What are the possible benefits and risks of participating?
Benefits: Taking part in the study will provide no direct benefit for you. The results from this study will help us to better understand how food changes our appetite and may help us to better treat future patients who suffer from obesity. If any of the screening questionnaires or blood tests reveal any medical problems (e.g. diabetes, kidney or liver problems), your GP will be

informed so that they can coordinate you further care, arrange any further tests, and refer you on to Hospital Doctors if necessary.

Risks:
Nutrient infusion: The nutrients infused into your gut are naturally produced in your gut after eating peas or chickpeas. They are generally not found to be linked to any side effects. Blood cannulation: Insertion of the cannula into your arms on each of the study visits may cause minor discomfort or superficial bruising. Risk associated with tube placement: If you take part in this study, you will have an ileal and duodenal tube placement under fluoroscopy. These procedures use ionising radiation to form images of your body and help your doctor position the tubes correctly. Ionising radiation may cause cancer many years or decades after the exposure. Everyone is at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening to you. During tube placement and removal, minor discomfort in the back of the throat occurs in the majority of patients and may result transiently in a sore mouth, thirst, swallowing difficulties, or hoarseness. For most subjects, the discomfort decreases once meals are consumed with the tube in place. Rare risks were observed associated with Tube Misplacements.

Where is the study run from?
NIHR Imperial Clinical Research Facility, Hammersmith Hospital, UK

When is the study starting and how long is it expected to run for?
January 2023 to January 2028

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

Who is the main contact?
Dr Mingzhu Cai (public), m.cai18@imperial.ac.uk/gutinfusion@imperial.ac.uk
Prof. Gary Frost (scientific), g.frost@imperial.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Mingzhu Cai

ORCID ID
https://orcid.org/0000-0002-1474-0224

Contact details
Imperial College London, 7th Floor Commonwealth Building, Imperial College Hammersmith Campus, DuCane Road
London
United Kingdom
W12 0NN
+44 (0)7395757128
m.cai18@imperial.ac.uk

Type(s)
Scientific, Principal investigator

Contact name
Prof Gary Frost

ORCID ID
https://orcid.org/0000-0003-0529-6325

Contact details
Imperial College London, 6th Floor Commonwealth Building, Imperial College, Hammersmith Campus, DuCane Road
London
United Kingdom
W12 ONN
+44 (0)20 7594 0959
g.frost@imperial.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
349450

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 66409, Biotechnology and Biological Sciences Research Council Grant Code BB/X018857/1

Study information

Scientific Title
Optimising gastrointestinal hormone and satiety responses through targeted delivery of metabolites to the human gut

Study objectives
Infusion of legume digestion-related nutrients into the stomach, duodenum, and ileum will enhance gut hormone and satiety responses compared to the infusion of saline in healthy subjects.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/02/2025, London – Surrey Borders (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 (0)2071048057; surreyborders.rec@hra.nhs.uk), ref: 25/LO/0050

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Investigating gut hormone and satiety responses

Interventions
15 healthy volunteers will attend a screening and a 3-day inpatient visit. During the main visit, two nasoenteric tubes will be inserted through nostrils into the ileum (day 1) and duodenum (day 2). Tube placements will be performed by a consultant radiologist. The locations of tubes will be verified by fluoroscopy. Once tubes are in place, participants will receive one of the following intervention/control treatments on day 2 and day 3 in a randomised order; randomisation will be performed using the 'sealed envelope' website by an independent researcher (i.e., not linked to the study):
• Intervention arm: Participants will consume an oral drink through a straw within 5 minutes (T0–5 min). This is composed of maltose and glucose, which are simple sugars. Then Infuscate D (a mixture of amino acids, the building bricks of proteins) will be infused to the duodenum from T30 to T120 minutes, and Infusate L (composed of simple sugars maltose, glucose and amino acids) to the ileum from 60 to 180 minutes. The drinks and infusates are composed of nutrients from food and are given in amounts that will reproduce the concentrations seen in the gut following food in our precious study.
• Control arm: Participants will consume an equal volume of a 0.9% saline solution as the drink. Then 0.9% saline solution will be infused into the duodenum and ileum at the corresponding rates and timeframes to match the intervention group.
Blood samples will be taken during the 0-180min period to measure appetite-related hormones, metabolite changes and glycaemic outcomes; Subjective appetite scores will be recorded; Urine samples will be collected to measure metabolite levels. After the infusion interventions, a pasta meal will be provided to measure food intake.

Intervention Type
Supplement

Primary outcome(s)
Plasma concentrations of gut hormones including gastric inhibitory polypeptide (GIP), glucagon-like peptide-1 (GLP-1), peptide Y (PYY), cholecystokinin (CCK) and oxyntomodulin (OXM) are measured by enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay (RIA) assays at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes

Key secondary outcome(s))
1. Appetite is measured using the visual analogue score (VAS) at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
2. Food intake is measured using an ad libitum pasta meal immediately after the 0-180 min intervention period
3. Plasma glucose concentrations are measured using the glucose oxidase-peroxidase

aminophenazone phenol (GOD-PAP) method at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
4. Serum insulin concentrations are measured using an ELISA method at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
5. Blood metabolites are measured using proton nuclear magnetic resonance profiling (1H NMR profiling) at -10, 0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180 minutes
6. Urine metabolites are measured using 1H NMR profiling on post-infusion samples (collected over 0-180min)

Completion date
01/01/2028

Eligibility

Key inclusion criteria
1. Male or female
2. Age between 18-65 years (inclusive)
3. Body mass index (BMI) of 18-30 kg/m2
4. Willingness and ability to give written informed consent and willingness and ability to understand, to participate and to comply with the study requirements

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Gastrointestinal disease e.g. inflammatory bowel disease or irritable bowel syndrome
2. Abnormal ECG
3. Screening blood results outside of normal reference values
4. Weight change of > = 5kg in the preceding 2 months
5. Current smokers
6. History of substance abuse and/or excess alcohol intake
7. Pregnancy
8. Diabetes
9. Cardiovascular disease
10. Cancer

11. Kidney disease
12. Liver disease
13. Pancreatitis
14. Started new medication within the last 3 months likely to interfere with energy metabolism, appetite regulation and hormonal balance, including: anti-inflammatory drugs or steroids, antibiotics, androgens, phenytoin, erythromycin or thyroid hormones.
15. Participation in a research study in the 12-week period prior to entering this study.
16. Any blood donation within the 12-week period prior to entering this study
17. Previous surgery on the bones inside the nose, or nasal airway obstruction

Any participants with the above conditions would already have an altered pattern of hormones and inflammatory molecules because of their disease process and would therefore give us confounding or misleading results.

Date of first enrolment
01/04/2025

Date of final enrolment
01/04/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Imperial Clinical Research Facility
Imperial Centre for Translational and Experimental Medicine
Imperial College Healthcare NHS Trust
Hammersmith Hospital Campus
Du Cane Road
London
United Kingdom
W12 0HS

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research council

Funder Name
Biotechnology and Biological Sciences Research Council

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 4	29/01/2025	04/03/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes