ISRCTN10822766 https://doi.org/10.1186/ISRCTN10822766

Effects of whey protein supplementation on gut permeability following exercise

Submission date	**Recruitment status**	[X] Prospectively registered
05/02/2025	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/02/2025	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
05/02/2025	Digestive System	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
During exercise, the blood supply to the gut is reduced and core body temperature is increased. Although these are normal physiological responses, they contribute to temporary increases in gastrointestinal (GI) permeability. This increase in GI permeability may contribute to gastrointestinal complaints frequently reported by athletes, such as nausea, diarrhoea and vomiting. Furthermore, changes in GI permeability can lead to elevated translocation of luminal contents into systemic circulation, which has been suggested as a potential contributing factor in exertional heatstroke.
There are a number of 'functional foods' or bioactive food products that can potentially improve (treat or prevent) gut injury and promote GI repair in the event of gut damage. Certain components in milk have been shown to have beneficial effects on gut integrity and permeability. The aim of this study is to determine whether supplementation with a whey protein concentrate can protect against exercise-induced increases in GI permeability.

Who can participate?
Healthy volunteers aged 18 to 65 years who are not taking any medication and meet all inclusion /exclusion criteria stated

What does the study involve?
Participants will come to the lab on six occasions over a period of roughly 6 weeks. This will be randomly allocated into two groups, one with the study protein and one with a placebo protein. Each arm will involve three visits, two of which involve exercise. Each group will last 15 days and will be separated by a 14-day washout period where no supplement will be taken.
Day 0: Participants undergo a 5-hour dual sugar absorption test (DSAT) and begin supplementation.
Day 7: Treadmill-based VO2max test - a standard incremental step test. Participants will run until they reach volitional failure, with expired gases (O2, CO2) measured breath-by-breath throughout. Heart rate and rate of perceived exertion (RPE) will also be measured every minute throughout the test.
Day 14: Final day of supplementation
Day 15: 20-min treadmill run at 80% of VO2max, on the same treadmill as the Day 7 trial. This will be preceded by a 5-minute warm-up (comprised of 1 minute walking at 4 km/h, 2 minutes at

a speed equivalent to 45% and 2 minutes at 55%, before immediately transitioning to 80% speed for 20 minutes). Heart rate and RPE will be measured every 5 minutes. Blood samples are taken pre-, post- and 1-h post-exercise, and a 5-h DSAT is performed post-exercise beginning immediately following exercise completion.
This is followed by a 14-day washout period (no supplement) before beginning the second group with the other supplement (crossover).

What are the possible benefits and risks of participating?
There are no direct benefits. Participants will receive two 2-week supplies of high-quality whey protein powder. Participants will also be provided with reasonable expenses (£50) for their time so they are not left out of pocket by taking part. All participants will also receive two VO2max reports, which would usually cost £70-150.
There is a mild-to-moderate risk of muscle soreness due to the exercise in the study. However, this will likely 'wear off' within 48 hours. The VO2max test involves maximal exertion. This can cause some people to feel nauseous or dizzy, however, this is a risk for all forms of maximal exercise. Any discomfort should be short-lived, and the participant will be aware that they are in full control, and can stop at any point. Such with the previous risks mentioned, exercise also has a small risk of muscle/joint injury. Participants will complete warmups and cool-downs to ensure this risk is minimised, and all necessary precautions will be taken to ensure this doesn't happen. Lastly related to exercise, any physical exertion comes with a risk of cardiac emergency, however, for those without underlying conditions, this risk is very low. The pre-screening health questionnaire is designed to ensure that anyone with such a condition is excluded from the study. Moreover, in the case of an emergency, a first aider will always be on hand, with access to a defibrillator. Using a needle, blood will be taken from a superficial vein in the forearm/elbow region. This may cause mild discomfort or pain, though this will be very short-lived. Some participants may feel faint following venepuncture. If this occurs, participants will be informed to let the researcher know and all processes will stop to allow them to recover. If needed, a first-aid-trained individual will be on hand. With all venepuncture, there is a small risk of infection at the site of entry. The researcher will be a certified phlebotomist and will follow all necessary hygiene procedures to ensure that this risk is minimised.

Where is the study run from?
University of Kent (UK)

When is the study starting and how long is it expected to run for?
October 2024 to August 2025

Who is funding the study?
1. Volac Whey Nutrition Limited (UK)
2. University of Kent (UK)

Who is the main contact?
William Searle, ws215@kent.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Mr William Searle

ORCID ID
https://orcid.org/0000-0002-5132-2312

Contact details
G05 Chipperfield Building
University of Kent
Canterbury
United Kingdom
CT2 7PE
+44 (0)1227 764000
ws215@kent.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
UoK SSES REAG Ref No. 75_2024

Study information

Scientific Title
Effects of whey protein supplementation on exercise-induced increases in gut permeability

Study objectives
The trial protein will reduce exercise-induced increases in gut permeability.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 06/12/2024, University of Kent SSES Research Ethics and Advisory Group (REAG) (University of Kent, Chipperfield Building, Kent, Canterbury, CT2 7PE, United Kingdom; + 44 (0) 1227 816943; k.taylor-399@kent.ac.uk), ref: 75_2024

Study design
Single-centre interventional double-blinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Exercise-induced increases in gut permeability

Interventions
1. Trial whey protein concentrate
2. Placebo (also whey-based protein)

Treatments will be administered using a randomised, double-blind design. Participants will consume 40 g of their assigned protein supplement daily for 2 weeks (from day 0 to 14 of each crossover arm). Following completion of the first crossover arm, participants will undergo a 2-week washout period where no supplement will be taken. Following this, the second arm will begin, following the same protocol as the first, but with the alternate protein supplement.

Intervention Type
Supplement

Primary outcome(s)
Lactulose:rhamnose ratio will be measured in urine samples taken at baseline (pre-supplementation) and post-exercise on main trials

Key secondary outcome(s))
1. Intestinal fatty-acid binding protein (I-FABP) will be measured by ELISA assays in blood samples taken pre-, post- and +1 h post-exercise
2. Bacterial load will be measured by qPCR on blood samples taken pre-, post- and +1 h post-exercise
3. Soluble CD14 (sCD14) concentration will be measured by ELISA assays in blood samples taken pre-, post- and +1 h post-exercise
4. WBC differentiation will be immediately performed on whole blood samples taken pre-, post- and 1-h post-exercise on main trial days

Completion date
31/08/2025

Eligibility

Key inclusion criteria
1. Male or female
2. 18-65 years old

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. Disease of the GI tract
2. Renal, hepatic, endocrine (including diabetes mellitus), cardiac, pulmonary, pancreatic, neurologic or biliary disorders
3. Intolerance or any known or suspected hypersensitivity (allergy) to study products/ingredients
4. Recent use of antibiotics (within 1 month of study)
5. Current, or recent, use of certain medications (NSAIDs)
6. Current, or recent, use of certain supplements (as per the researcher's determination) that could influence study measures or outcomes (such as pre or probiotics, for example)
6. Females who are pregnant, lactating, or planning to become pregnant during the study period
7. Enrolment in any other similar trial within 3 months prior to recruitment
8. Investigator's determination of unsuitability for trial participation

Date of first enrolment
01/03/2025

Date of final enrolment
01/07/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Kent
Chipperfield Building, Park Wood Road, University of Kent
Canterbury
United Kingdom
CT2 7PE

Sponsor information

Organisation
University of Kent

ROR

https://ror.org/00xkeyj56

Funder(s)

Funder type
Industry

Funder Name
Volac Whey Nutrition Limited

Funder Name
University of Kent

Results and Publications

Individual participant data (IPD) sharing plan
The data generated during this study will be available upon request from William Searle (ws215@kent.ac.uk), Professor Glen Davison (G.Davison@kent.ac.uk) or Dr Megan Judge (M.L.Judge@kent.ac.uk) after completion and publication of study results (de-identified participant data), and may be used for secondary analysis or as part of meta-analyses and other relevant and legitimate scientific uses only. All data will be fully anonymised so that it will not be possible for the identity of participants to be known or deduced. The researchers will ask those requesting data sharing to provide a brief research proposal on how they wish to use the data. This will then form the basis of a data-sharing agreement (if necessary/appropriate to do so), which will clearly detail the criteria for data access and conditions for research use. The researchers will also include a requirement for due acknowledgement and/or co-authorship (if/when appropriate) and acknowledgement of the funder for supporting the original study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes