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The effect of a ketone drink on blood glucose levels in people with type 2 diabetes

Submission date
16/02/2024

Recruitment status
No longer recruiting

Registration date
19/02/2024

Overall study status
Completed

Last Edited
28/01/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Ketones are naturally produced by our body and can affect our blood sugar levels. Ketones could be important in the treatment of type 2 diabetes (T2D). The purpose of this research is to determine if a ketone drink can lower blood sugar in people with T2D following a meal. This research will provide new knowledge about the regulation of blood sugar. This may also inform if ketone drinks could be used as a treatment for T2D.

Who can participate?
We are inviting 12 adults between the ages of 41 and 70 with T2D to take part.

What does the study involve?
The study involves:
A short telephone call with the researcher
A screening visit with a questionnaire and a blood sample
Two 'priming visits' to our laboratory to ingest a 'labelled water' drink, each followed by a 'test visit' the next day
Eating a meal on the day before the test visits
Skipping breakfast before your test visits
Resting on a bed for 13 hours on each test visit when a small amount of glucose (sugar) will be infused into the arm and regular blood samples will be taken
Consuming 2 ketone drinks on one of the test visits
Consuming 2 milkshakes on both of the test visits

What are the possible benefits and risks of participating?
We cannot promise any specific benefits to participants personally. At the end of the study, participants can request results about how their body responded to the ketone drink. The ketone drink is commercially available so there may be financial benefit to companies that sell ketones in the future.
The risks involved in this study are minimal. We will not ask participants to change any of their usual treatment or care. If we find any results that could indicate a previously undiagnosed disease or illness, we will tell participants and advise them to speak to their GP. The ketone drink is commercially available (https://www.deltagketones.com) and has been given to people with

type 2 diabetes before with no side effects. Participants will skip breakfast on each of the test days so may feel hungry for a few hours. The milkshake we give after 2.5 hours of the visit should stop them feeling hungry for the next 4.5 hours of the visit until they receive another milkshake. We will give them something to eat and drink before they go home. Insertion of needles may cause some temporary discomfort. The investigators are trained and experienced in all aspects of these procedures. Any concerns that participants may have about any of the procedures will be addressed in full by the researchers prior to participants giving their consent to participate.

Where is the study run from?
Nutritional Physiology Research Unit, St Luke's Campus, University of Exeter, Exeter, UK.

When is the study starting and how long is it expected to run for?
November 2023 to January 2026

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Professor Francis Stephens, F.B.Stephens@exeter.ac.uk
Dr George Pavis, G.Pavis@exeter.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06324669

Protocol serial number
4765060

Study information

Scientific Title
Investigating the blood glucose lowering effect of exogenous ketone ingestion in people with type 2 diabetes

Study objectives
It is hypothesised that the antilipolytic effect of β-hydroxybutyrate reduces endogenous glucose production and/or increases glucose clearance

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/11/2023, FHLS Sports and Health Sciences Ethics Committee (University of Exeter, Exeter, EX1 2LU, United Kingdom; +44 300 555 0444; cgr-reg@exeter.ac.uk), ref: 4765060

Primary study design
Interventional

Study design
Single-centre interventional randomized single-blind placebo-controlled crossover study

Study type(s)
Other

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
Participants will visit the laboratory for baseline screening to assess their eligibility. Thereafter they will undergo 2 trials, with trial order (ketone or placebo) randomised using excel ‘rand’ function. On day 1 participants will visit the laboratory to consume ‘heavy water’ (deuterium oxide). On day 2 participants will return and undergo a 13 h test day. After placement of cannulas and the initation of stable isotope tracer infusion, participants will receive a 100 mL

flavoured drink containing 0.3 g/kg ketone monoester ((R)-3-hydroxybutyl (R)-3-hydroxybutyrate; ΔG®, University of Oxford; https://www.deltagketones.com) or maltodextrin placebo with stevia and bitter agent to flavour match. The ketone ester is commercially available, is not contraindicated for diabetes medication, the dose is within the guidelines, and it has been used several times before in patients with type 2 diabetes. Participants will then consume a mixed macronutrient study beverage (Ensure Plus, Abbott Nutrition), and have blood samples taken at regular intervals for 4 h. Participants will receive a second dose of their allocated condition (ketone or placebo), consume a second mixed macronutrient beverage, and have blood samples taken for a second 4 h period.

Intervention Type
Supplement

Primary outcome(s)
Rate of endogenous glucose production over 4 hours in response to a meal measured by blood sample

Key secondary outcome(s)
1. Total rate of glucose appearance measured using the change in glucose enrichment /concentration over 4 and 8 hours following a meal
2. Exogenous rate of glucose appearance measured using the change in glucose enrichment /concentration over 4 and 8 hours following a meal
3. Total rate of glucose disappearance measured using the change in glucose enrichment /concentration over 4 and 8 hours following a meal
4. Rate of gluconeogenesis measured using the change in glucose enrichment/concentration over 4 and 8 hours following a meal
5. Rate of glycogenolysis measured using the change in glucose enrichment/concentration over 4 and 8 hours following a meal
6. Beta-cell function using dynamic modelling of insulin/c-peptide secretion over 4 and 8 hours following a meal
7. Insulin concentration using ELISA assay over 4 and 8 hours following a meal
8. glucagon concentration using ELISA assay over 4 and 8 hours following a meal
9. GLP-1 using ELISA assay over 4 and 8 hours following a meal
10. GIP concentration using ELISA assay over 4 and 8 hours following a meal
11. Glycerol concentration using colorimetric assay over 4 and 8 hours following a meal
12. Free fatty acids using colorimetric assay over 4 and 8 hours following a meal
13. Ketone concentration using colorimetric assay over 4 and 8 hours following a meal
13. Energy expenditure using indirect calorimetry over 4 and 8 hours following a meal

Completion date
31/01/2026

Eligibility

Key inclusion criteria
1. Aged 41-70 years old
2. Body mass index 27-40 mg/m²
3. Type 2 diagnosis for more than 1 year
4. HbA1c >6%

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
41 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
15

Key exclusion criteria
1. Currently following ketogenic diet
2. Use of insulin
3. HbA1c >10%
4. Recent weight loss (>5kg in 6 months)
5. Recent eGFR <30mL/min
6. Heart failure
7. Substance abuse
8. Cancer
9. Myocardial infarction within 6 months
10. Pregnancy or consideration of
11. Use of antipsychotic drugs

Date of first enrolment
15/03/2024

Date of final enrolment
28/01/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Exeter
Stocker Road

Exeter
United Kingdom
EX4 4PY

Sponsor information

Organisation
University of Exeter

ROR
https://ror.org/03yghzc09

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

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
The anonymised datasets generated during and/or analysed during the current study will be stored in an institutional and/or publicly available repository, such as FigShare

IPD sharing plan summary
Stored in publicly available repository