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Investigating the potential health benefits of ergothioneine supplementation for people with metabolic syndrome

Submission date
21/08/2020

Recruitment status
Recruiting

Registration date
10/02/2021

Overall study status
Ongoing

Last Edited
02/05/2023

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:
Ergothioneine is an amino acid found commonly in mushrooms. It acts as an antioxidant like other dietary nutrients such as vitamin C, vitamin E and selenium. Metabolic syndrome is a group of risk factors that increase a person's risk of diabetes and heart disease. The aim of this study is to investigate the potential health benefits of 12-weeks ergothioneine supplementation in people with metabolic syndrome. Specifically, the study will investigate if ergothioneine supplementation will alter markers of metabolism, oxidative stress, inflammation and liver function in the blood.

Who can participate?
Adults with metabolic syndrome

What does the study involve?
Participants will be asked to take a single capsule daily for 12 weeks. Participants will be asked to visit the study site three times: at the start, after 6 weeks, and after 12 weeks of supplementation. This will be to complete questionnaires, provide blood samples, and have their height, weight, waist circumference and blood pressure measured.

What are the possible benefits and risks of participating?
Participants will receive measurements of body weight, height, waist circumference and blood pressure and assessments of oxidative stress, inflammatory markers and liver health. Potential benefits may be improvements in metabolic syndrome risk factors.
Risks to participating are considered minimal. The supplemental doses of ergothioneine (5/30 mg/day) being tested are considered safe under these conditions and are well below the safety limit (800 mg/kg body weight per day—e.g. 56,000 mg/day for a 70 kg adult) established by the European Food Safety Authority in 2016.

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

When is the study starting and how long is it expected to run for?
June 2020 to June 2027

Who is funding the study?
University of Leeds (UK)

Who is the main contact?
Dr. J. Bernadette Moore
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
A randomised, double-blind, placebo-controlled pilot study investigating the effects of 12 weeks ergothioneine supplementation on serum oxidative, inflammatory, and metabolic markers in people with metabolic syndrome

Acronym
ErgMS

Study objectives
In order to establish primary and secondary outcomes and power required for a definitive randomised control trial, the aim is to address three primary questions in this pilot study:
1. Is it feasible to recruit and supplement people with metabolic syndrome with ergothioneine for 12 weeks?
2. What, if any, changes in metabolic syndrome risk factors, serum markers of oxidative stress (lipid peroxidation), inflammation and liver function can be observed in response to ergothioneine supplementation?
3. Are there changes in the serum metabolome in response to ergothioneine supplementation?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/12/2020, Engineering and Physical Sciences Faculty Research Ethics Committee (University of Leeds, LS2 9NL; no telephone number provided; EPSResearchEthics@leeds.ac.uk), ref: MEEC 20-007

Study design

Single-centre randomised double-blind placebo-controlled three-arm parallel pilot interventional trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Metabolic syndrome

Interventions
Consenting participants will be randomised in a double-blind fashion to one of three groups to receive either placebo (0 mg ergothioneine), 5 mg ergothioneine, or 30 mg ergothioneine for consumption as daily capsules (one per day) for 12 weeks. Participants will give blood samples and undergo anthropometric measurements at three timepoints, baseline, 6 weeks and 12 weeks.

Randomisation and group allocation will be done based on predefined random allocation lists using simple stratification for sex (one each for males and females), with a block size of 6 and allocation list of 2:2:2; aiming to recruit 108 participants for n=36 in each group. The randomisation schedule will be carried out by a collaborator who will not be involved in any other part of this trial and who will also be blinded to the dose allocation ('A', 'B' or 'C') designated by the manufacturer and provided in a sealed envelope. The collaborator will maintain the lists matching screening IDs to randomisation IDs, along with the manufacturer's sealed envelope for the duration of the trial. This envelope will only be opened before study completion in the case of a serious adverse event.

Intervention Type
Supplement

Primary outcome(s)
Current primary outcome measures as of 14/05/2021:
1. Recruitment and completion will be measured in the numbers of participants enrolling and completing all study visits
2. Supplementation compliance will be measured both by capsule counting (participants returning packaging and untaken supplements) and the measurement of ergothioneine in serum by LC-MS at baseline, 6 weeks and 12 weeks

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Previous primary outcome measures:
1. Recruitment and completion will be measured in the numbers of participants enrolling and completing all study visits
2. Supplementation compliance will be measured both by capsule counting (participants returning packaging and untaken supplements) and the measurement of ergothioneine in plasma by HPLC at baseline, 6 weeks and 12 weeks

Key secondary outcome(s))

Current secondary outcome measures as of 31/08/2021:
1. Levels of malondialdehyde (MDA), as a primary serum marker of oxidative stress (specifically, lipid peroxidation), will be measured by high-performance liquid chromatography (HPLC) at baseline, 6 weeks, and 12 weeks
2. Serum levels of tumour necrosis factor-alpha (TNF-α), as a marker of inflammation, will be measured by enzyme-linked immunosorbent assay (ELISA) at baseline, 6 weeks, and 12 weeks
3. Serum levels of nuclear factor erythroid 2-related factor 2 (Nrf2), as a marker of inflammation, will be measured by enzyme-linked immunosorbent assay (ELISA) at baseline, 6 weeks, and 12 weeks
4. C-reactive protein (CRP) will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks
5. NADPH oxidase 4 (NOX4) expression will be measured by real-time quantitative polymerase chain reaction (qPCR) at baseline, 6 weeks, and 12 weeks
6. Serum alanine transaminase (ALT), as a marker of liver function, will be measured by commercial assay kit at baseline, 6 weeks, and 12 weeks.
7. Height will be measured by stadiometer at baseline
8. Body weight will be measured by beam scale at baseline, 6 weeks and 12 weeks
9. Blood pressure will be measured by blood pressure monitor at baseline, 6 weeks and 12 weeks
10. Waist circumference will be measured by tape at baseline, 6 weeks and 12 weeks
11. Triglycerides (TAG) will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks
13. Cholesterol-high density lipoprotein (HDL) will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks.
14. Fasting glucose will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks
15. Platelet characteristics (including function, surface markers of platelet activation, platelets subsets, platelet ROS generation and platelet-leukocyte aggregates) will be assessed in whole blood by multicolour flow cytometry at baseline, 6 weeks, and 12 weeks
16. Serum metabolites will be measured by liquid chromatography-mass spectrometry (LC-MS) at baseline, 6 weeks, and 12 weeks

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Previous secondary outcome measures as of 16/03/2021:
1. A primary serum marker of oxidative stress (specifically, lipid peroxidation), malondialdehyde (MDA), will be measured by high-performance liquid chromatography (HPLC) at baseline, 6 weeks, and 12 weeks
2. Serum markers of inflammation, tumour necrosis factor-alpha (TNF-α) will be measured by enzyme-linked immunosorbent assay (ELISA) at baseline, 6 weeks, and 12 weeks. Nuclear factor erythroid 2-related factor 2 (Nrf2) will be measured by immune blotting at baseline, 6 weeks, and 12 weeks. C-reactive protein (CRP) will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks. NADPH oxidase 4 (NOX4) will be measured by real-time polymerase chain reaction (qPCR) at baseline, 6 weeks, and 12 weeks
3. Serum markers of liver function, Alanine transaminase (ALT), will be measured by commercial assay kit at baseline, 6 weeks, and 12 weeks.
4. Metabolic syndrome risk factors will be measured at baseline, 6 weeks and 12 weeks. Height will be measured by stadiometer at baseline. Body weight, blood pressure, waist circumference will be measured by beam scale, blood pressure monitor and tape respectively. Triglycerides (TAG), cholesterol-high density lipoprotein (HDL) and fasting glucose will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks
5. Serum metabolites will be measured by liquid chromatography-mass spectrometry (LC-MS) at baseline, 6 weeks, and 12 weeks

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Previous secondary outcome measures:
1. A primary serum marker of oxidative stress (specifically, lipid peroxidation), malondialdehyde (MDA), will be measured by high-performance liquid chromatography (HPLC) at baseline, 6 weeks, and 12 weeks
2. Serum markers of inflammation, tumour necrosis factor-alpha (TNF-α) and nuclear factor erythroid 2-related factor 2 (Nrf2) will be measured by enzyme-linked immunosorbent assay (ELISA) at baseline, 6 weeks, and 12 weeks. C-reactive protein (CRP) will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks. NADPH oxidase 4 (NOX4) will be measured by real-time polymerase chain reaction (qPCR) at baseline, 6 weeks, and 12 weeks
3. Serum markers of liver function, Alanine transaminase (ALT), will be measured by commercial assay kit at baseline, 6 weeks, and 12 weeks.
4. Metabolic syndrome risk factors will be measured at baseline, 6 weeks and 12 weeks. Height will be measured by stadiometer at baseline. Body weight, blood pressure, waist circumference will be measured by beam scale, blood pressure monitor and tape respectively. Triglycerides (TAG), cholesterol-high density lipoprotein (HDL) and fasting glucose will be measured in whole blood using a rapid point-of-care multi-assay blood analyser at baseline, 6 weeks and 12 weeks
5. Serum metabolites will be measured by liquid chromatography-mass spectrometry (LC-MS) at baseline, 6 weeks, and 12 weeks

Completion date
01/06/2027

Eligibility

Key inclusion criteria
Participants must be 18-70 years old, overweight or obese, and have risks of metabolic syndrome, defined by presenting with at least two of the six following criteria:
1. BMI >25 kg/m²
2. Abdominal obesity: high waist circumference (Asian/Asian British - men ≥90 cm; women ≥80 cm; White and all other ethnic groups - men ≥94 cm, women ≥80 cm)
3. Fasting glucose ≥100 mg/dl (5.6 mmol/l) or treatment for elevated blood glucose
4. Blood pressure ≥130/85 mmHg or treatment for elevated blood pressure
5. Triglycerides ≥150 mg/dl (1.7 mmol/l) or treatment for elevated triglycerides
6. Cholesterol-high density lipoprotein (HDL-C) < 40 mg/dl (1.0 mmol/l) for male or < 50 mg/dl (1.3 mmol/l) for female or treatment for low HDL-C

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Key exclusion criteria
1. Participants who are under 18 years old or over 70 years
2. Women who are pregnant or lactating
3. Participants who smoke
4. Participants who consume ≥28 units of alcohol per week (28 units = ~10 medium glasses of wine (175 mL) or ~10 pints of beer/cider)
5. Participants who have taken dietary/antioxidant supplements within the last 4 months (adequate washout period)
6. Participants who have newly implemented a diet or exercise regime (≥150 min/week moderate aerobic exercise or ≥75 min/week vigorous aerobic exercise) aimed at weight loss
7. Participants who have gained or lost weight of >3 kg or more in last month
8. Participants who are following lifestyle change advice
9. Diagnosis of liver disease, diabetes, heart disease, kidney disease or intestinal disorders (Crohn’s disease, short bowel syndrome, pancreatic insufficiency, cystic fibrosis, tropical sprue, Whipple's disease, chronic pancreatitis, gastrojejunostomy, surgical treatment for obesity, cholestasis, biliary atresia, parasitic infections)
10. Diagnosis of cancer or end of cancer treatment within 2 years
11. Participants taking prescription anti-inflammatory medicines (occasional aspirin, paracetamol, ibuprofen use acceptable)
12. Participants who have been diagnosed with a blood borne disease (HepB, HIV etc.)
13. Participants receiving antibiotic treatment within last month or 3 courses within the last 6 months
14. Participating in other clinical trials that may influence outcomes
15. Participants who are impaired in cognition or cannot complete the trial independently
16. Participants who have difficulties in understanding written and/or verbal English
17. Participants who cannot come to the University
18. Participants who are unwilling or unable to provide informed consent
19. Participants who can not wear a face mask during the visit

Date of first enrolment
01/04/2024

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Leeds
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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
University/education

Funder Name
University of Leeds

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

IPD sharing plan summary

Available on request