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Effects of exercise and quercetin on DNA integrity

Submission date	Recruitment status	[ ] Prospectively registered
20/02/2025	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
26/02/2025	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
10/04/2025	Genetic Diseases	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
As we get older, our risk of developing diseases like cancer, heart disease, and brain disorders increases. Exercise is known to help slow down ageing by making positive changes to our DNA. This study aims to see how high-intensity exercise (HIE) and a natural supplement called quercetin affect DNA and the ageing process in healthy males.

Who can participate?
Healthy males aged 30-45 years who live in the UK or Ireland are invited to take part in the study.

What does the study involve?
Participants will first undergo fitness testing at Ulster University Belfast, where their height, weight, and fitness levels will be measured. They will then perform high-intensity exercise and provide blood samples before and after exercise and supplementation. Participants will take either quercetin or a placebo for 21 days, with a one-week break between treatments.

What are the possible benefits and risks of participating?
Participants will contribute to important research on ageing and may gain insights into their own fitness levels. Risks include muscle injury, heart issues, nausea, fainting, infections, and discomfort from blood sampling. The research team has taken steps to minimize these risks.

Where is the study run from?
The study is conducted at the Human Performance Lab at Ulster University Belfast (UK)

When is the study starting and how long is it expected to run for?
September 2022 to May 2025

Who is funding the study?
DoNotAge.org
Ulster University (UK)

Who is the main contact?
Ciara Juan, PhD Researcher (Juan-CA@ulster.ac.uk)
Prof. Gareth Davison, Chief Investigator (gw.davison@ulster.ac.uk)

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Protocol serial number
REC/23/0020

Study information

Scientific Title

Exercise and quercetin in ageing-associated DNA repair and epigenetic modifications

Study objectives
Exercise and quercetin, individually and in combination, activate DNA repair pathways

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 30/12/2022, Ulster University Research Ethics Committee (UREC) (York Street, Belfast, BT15 1ED, United Kingdom; +44 (0)28 95365028; e.bell2@ulster.ac.uk), ref: REC/23/0020

Study design
Single-center interventional double-blind randomized placebo-controlled crossover trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of genome instability in healthy middle-aged men

Interventions
All participants completed a three-week intervention with an oral quercetin supplement (1000 mg per day) and another three-week intervention with a placebo, separated by a 1-2 weeks washout period. Laboratory technicians generated random numbers using the R programming language, ensuring that each participant had an equal chance of being placed in any group, minimising bias in the study design. Blinding was unknown to the PhD student who gathered data.

Intervention Type
Supplement

Primary outcome(s)
Current primary outcome measures as of 10/04/2025:
The primary outcome measures are assessed at baseline before quercetin, baseline before placebo, after 3 weeks of quercetin, after 3 weeks of placebo, after exercise with quercetin, and after exercise without quercetin, except where stated otherwise:
1. DNA strand breaks measured using single-cell gel electrophoresis
2. Oxidised purines measured using single-cell gel electrophoresis with formamidopyrimidine DNA glycosylase (FPG) enzyme incubation
3. DNA double-strand breaks measured using immunofluorescence for γH2AX and 53BP1 foci
4. Lipid damage measured using the spectrophotometric lipid hydroperoxide assay
5. DNA repair gene expression (SIRT1, SIRT6, PARP1, RAD51, OGG1, XRCC1, etc.) measured using RT-qPCR
6. Telomere length measured using qPCR at baseline before quercetin, baseline before placebo, after 3 weeks of quercetin, and after 3 weeks of placebo
7. Plasma quercetin levels using HPLC-mass spectrometry

Previous primary outcome measures:
The primary outcome measures are assessed at baseline before quercetin, baseline before placebo, after 3 weeks of quercetin, after 3 weeks of placebo, after exercise with quercetin, and after exercise without quercetin, except where stated otherwise:
1. Total DNA damage measured using single-cell gel electrophoresis
2. Single-strand break DNA damage measured using single-cell gel electrophoresis with formamidopyrimidine DNA glycosylase (FPG) enzyme incubation
3. Double-strand break DNA damage measured using dual staining immunohistochemistry for γH2AX and 53BP1 foci
4. Lipid damage measured using the spectrophotometric lipid hydroperoxide assay
5. DNA repair gene expression (SIRT1, SIRT6, PARP1, RAD51, OGG1, XRCC1, etc.) measured using RT-qPCR
6. Telomere length measured using qPCR at baseline before quercetin, baseline before placebo, after 3 weeks of quercetin, and after 3 weeks of placebo

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/05/2025

Eligibility

Key inclusion criteria
1. Male: Menstrual cycle-related hormonal variations in women are known to affect the molecular pathways associated with the DNA damage repair response.
2. Lightly active: Having a VO2max of <50ml/kg/min. Athletes and very fit individuals tend to have a blunted response to exercise which may be due to genetic factors or exercise training effects.
3. Of normal weight: Having a BMI of 18.5 to 24.9. Overweight/obese participants also have a blunted response to exercise partly due to impaired blood flow.
4. Omnivore: Vegans have a differential SIRT1 response to acute exercise (Potthast et al., 2020) which may be due to their blood and cell antioxidant status.
5. Non-smoker: Smokers are known to have differential hormonal, antioxidant, and inflammatory status that may affect the exercise and supplementation response.
6. Not a heavy drinker: Not exceeding 14 units of alcohol per week. Heavy drinkers are also known to have differential hormonal, antioxidant, and inflammatory status.
7. Not on any medication or supplementation affecting response to exercise.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 years

Upper age limit
45 years

Sex
Male

Total final enrolment
13

Key exclusion criteria
1. Smoking: Smokers are known to have differential hormonal, antioxidant, and inflammatory status that may affect the exercise and supplementation response.
2. Exceeding 14 units of alcohol per week: Heavy drinkers are also known to have differential hormonal, antioxidant, and inflammatory status.
3. Working in night shift: SIRT1 regulates circadian rhythm and vice versa.
4. Having an infection: Respiratory tract infections, gastrointestinal issues, or any changes in inflammatory status affect the exercise response.
5. Having cardiovascular or metabolic disorders: These diseases are associated with impaired blood flow that affects exercise response.
6. Taking a clinically prescribed medicine: Medication can interfere with the associated molecular pathways.
7. Being an athlete or overly fit (VO2max >50ml/kg/min).

Date of first enrolment
01/08/2023

Date of final enrolment
30/03/2024

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
University of Ulster
York Street
Belfast
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BT15 1ED

Sponsor information

Organisation
University of Ulster

ROR
https://ror.org/01yp9g959

Funder(s)

Funder type
Charity

Funder Name
DoNotAge.org

Funder Name
Ulster University

Alternative Name(s)
University of Ulster, Ulster, Ulster Uni, Ollscoil Uladh, Ulstèr Universitie, Ulstèr Varsitie, UU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
For each participant, his own unique, individual dataset generated during and/or analysed during the current study, such as values for telomere length and DNA damage and repair, are/will be available to him upon request from Ciara Juan juan-ca@ulster.ac.uk beginning March 2025 onwards through the participant's email. The datasets generated and/or analysed as a group during the current study will be published as a supplement to the results publication without identifying the participants. All participants consented to the use of their data for research purposes.

IPD sharing plan summary
Available on request, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			24/02/2025	No	Yes