Sport and Exercise Sciences Research Institute
Faculty of Life and Health Sciences

PARTICIPANT INFORMATION SHEET

Research Title: Exercise and quercetin in ageing-associated DNA repair and epigenetic modifications

Invitation

You are being invited to take part in this research project, as you are an adult male. Before you decide to do so, it is important you understand why the research is being done and what it will involve. Please take time to read the following information carefully, discuss it with us, and feel free to ask any related questions. Ask us if there is anything that is not clear, or if you would like more information. Please take time to decide whether or not you wish to take part. Thank you for reading this information.

What is the purpose of the study?

As we age, the chances of getting the so-called "diseases of ageing" (cancer, heart disease, brain degeneration, obesity and muscle disorders, etc.) greatly increase. Exercise is known to be a good "anti-ageing" strategy, brought about by a number of biological mechanisms, one of which is making changes to DNA. Ageing is characterised by unfavorable changes in our DNA, but these changes can potentially be reversed through exercise and supplements that mimic exercise.

We hope to observe these changes in DNA after high-intensity exercise (HIE) and taking a natural supplement (quercetin) in a sample of healthy males. The overall aim of this investigation is to answer the question: *What are the immediate and short-term effects of exercise and quercetin, individually and in combination, on DNA and the related ageing process?*

What is quercetin?

Quercetin is a natural plant-based food product that may be important to keep our DNA healthy. It has been shown, depending on its concentration, to improve DNA repair, and it shows some promise at changing cell DNA for the better. Previous studies found quercetin to be well-tolerated following human intake, and effective at improving exercise performance in healthy adults.

Why have I been chosen?

All healthy males aged 30-45 who are residents of the UK or Ireland are invited to participate.

What do I have to do?

Stage 1 - Fitness Testing: You will be invited to the Human Performance Lab at Ulster University Belfast, where your height and weight will be recorded. You will then be asked to complete a fitness test on a bike. The exercise intensity will be set at 60RPM and 100W, and the intensity of exercise will increase every 3 minutes by 50W until you decide to voluntarily stop exercising. While you are exercising, you will be asked to wear a plastic mouthpiece, and this will allow us to measure the amount of oxygen that you are breathing during the exercise test. You will also be asked to wear a heart rate monitor on your wrist and a strap around your waist so we can record your heart rate. You will be asked to stop participating in any form of exercise and stop drinking alcohol or caffeine or taking any antioxidant supplements (multivitamins, vitamin C, vitamin E etc. – please ask if you need any

clarification) for 48 hours before you come to the lab. If you are on long-term antioxidant supplementation, you are required to stop taking the antioxidant(s) for up to 6 weeks before exercise testing.

Stage 2 – Experimental Testing: You will be required to provide blood samples before and after high-intensity exercise, and before and after supplementation.

HIE. You are required to perform high-intensity exercise by completing 4 x 4-minute cycling bouts, with each bout requiring 90-95% of effort separated by 3-minutes of relaxed recovery at 70% effort.

Blood Samples. A total of eight venous blood samples will be collected from the forearm: before and following exercise, before and following quercetin ingestion, and before and following exercise with placebo ingestion. In each blood draw, a total of 34 ml of whole blood will be taken. For the whole study, a total of 272 ml of whole blood will be taken.

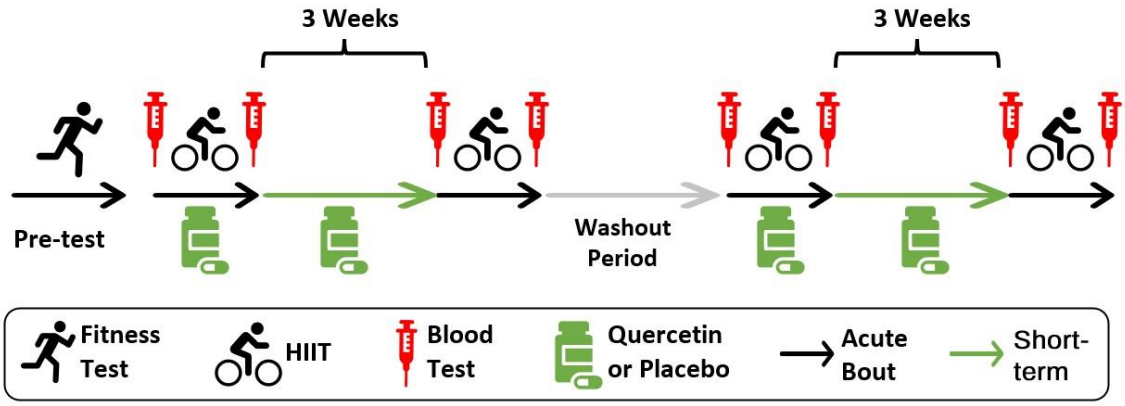
Supplementation. In a random order and unknown to both the participant and the researcher administering the supplements, each individual will be given either quercetin or a placebo to ingest. Pure quercetin and the placebo will be prepared by a Biotech company trusted by the University. The quercetin and the placebo will be in identical capsules.

Short-term Supplementation. In the main supplementation phase, each participant will take 1000 mg of quercetin per day for a total of 21 days. Up to three months of quercetin supplementation using 1000 mg has no adverse effects in healthy adults. In the placebo, you will take placebo pills containing rice flour for the same duration. Each participant will receive a 21-day supply of the capsules and daily reminders (via text message) to consume the capsules with breakfast.

Acute Supplementation. The acute supplementation period will include the ingestion of a single dose of either 1000 mg of quercetin or placebo, 1 hour before exercise, and this is based on a study showing increased plasma quercetin after one hour of ingestion. The acute supplementation phase will count as Day 1 of short-term supplementation and will continue thereafter for 21 days.

Washout/rest period. To avoid the first treatment affecting the next treatment, a rest period of 1 week between supplement interventions (quercetin and placebo) will be implemented, where no supplement or placebo will be administered.

Clinical Trial Design



Do I have to take part?

It is completely up to you to decide whether or not you take part. If you decide to participate, you will be given this information sheet to keep and you will be asked to provide contact details and sign a consent form. You have the right to withdraw from the study at any time without giving a

reason up until the point that the questionnaire is submitted. You can do so by contacting any of the research team on the email addresses provided. **A decision to withdraw, or a decision not to participate, will not have any implications whatsoever for you as a student at Ulster University.** If you withdraw from the study, stored samples will be destroyed in accordance with the Human Tissue Act regulations.

How will my data be treated and will my taking part in this study be kept confidential?

With each piece of data collected, it will be treated with the strictest of confidence, according to the principles outlined in the general data protection regulation (GDPR;2018). All data specifically will be stored on a password-protected/encrypted computer with only the researchers having access to this information. Anonymous codes will be used to protect the identify of participants. The confidential right of participants will be fully respected.

Privacy notice and sponsor compliance with GDPR and the Data Protection Act 2018

Ulster university is the managing organisation for this study. The university is committed to protecting the rights of individuals in accordance with the provisions of the General Protection Regulation (GDPR) and Data Protection Act (DPA). The data collected for this study will comply with the GDPR and DPA protocols.

The university will retain the necessary information on you in obligation to the protocols of GDPR and DPA and ensures that when no longer needed, data is disposed of in a timely and appropriate manner. We need to manage information and retain in specific way in order for the research to be reliable and accurate making your rights to access, change or move your information very limited. Please note, if you withdraw from the trial, your information already obtained will be kept. To safeguard your rights, we will use the minimum personal identifying information possible.

Health, care and other human research should serve the public interest. This means that we have to demonstrate that our research serves the interest of those within society as a whole. This is done by following university and appropriate UK policies and codes of practice. The only people who can obtain your information are those who contact you about the study or to carry out audits of the research within the university.

If you wish to make a complaint on how your personal data has been maintained, you can contact the universities Data Protection Officer in which they will investigate the manner. If you are not happy with the response or have not processed your personal data in a lawful way, you can complain to the Information Commissioners Office.

Our Data Protection Officer is Clare Jamison and is available to contact at c.jamison@ulster.ac.uk

Risks & Benefits to Participants

In all scientific studies, there are always risks that could occur during testing. These include muscular injury, heart complications, nausea, fainting, bacterial/viral infection, bloodborne diseases and bruising or discomfort from blood sampling. If you experience any of these, please let us know immediately.

The research team has taken all necessary steps to minimise these, including screening participants and training for safety protocols. All members of the team are certified and trained in conducting blood extraction, first aid/basic life support, and exercise training.

Note: If there are any changes in circumstances or medical status between completing the medical risk form and the beginning of the study, please let us know.

By participating in this study, you are contributing to the advancement of science by being part of an important research that will help determine mechanisms involved in ageing interventions. You are also taking the first steps in improving your own health by being aware of your fitness levels.

What if new information becomes available?

If new information becomes available during the course of the study, you will be kept informed, and any options or requests/requirements fully explained. New information could result in termination of the study, the withdrawal of certain participants, or modifications/amendments to the study.

What if something goes wrong?

It is very unlikely that something will go wrong during this research. However, the University take complaints and concerns seriously and has procedures in place for reporting, investigating, recording and handling them. The University is insured for its staff and students to carry out research involving people however this does not extend to non-negligent harm. The University knows about this research project and has approved it. Further details on insurance can be found in the University's research indemnity statement. Ask us if you would like a copy.

What will happen to the results of the research study?

It is intended that the findings from this study will be published in scientific or medical journals and presented at conferences. You will **not** be identified in any report or publication.

Who has reviewed this study?

The study has received ethical approval from Ulster University Research Ethics Committee.

Thank you for your interest in this study, and if you have further questions, please feel free to contact the following:

Ciara Juan, PhD Researcher Juan-CA@ulster.ac.uk
Prof. Gareth Davison – Chief Investigator gw.davison@ulster.ac.uk