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Using lutein-fortified yoghurt as a vehicle to deliver lutein to humans – a bioavailability study

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13/06/2022

Recruitment status
No longer recruiting

Registration date
28/06/2022

Overall study status
Completed

Last Edited
06/09/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Xanthophyll carotenoids (oxygen-containing, plant-based pigments that give fruits and vegetables their bright colours) are an important part of a healthy diet. Examples of carotenoid include lutein (which gives the yolk of an egg its yellow colour, lycopene which gives tomatoes their red colour, and beta-carotene which is why carrots are orange). Our body cannot make carotenoids and so we must get them from our diet or from food supplements. Unfortunately, the evidence to date says that we don't eat enough of these nutrients every day to reap their benefits.

Research from our Centre (and others) has shown that greater consumption of these nutrients from food supplements can improve levels of these nutrients in blood and tissue. This in turn can positively impact our day-to-day function (e.g. visual and cognitive performance primarily due to their antioxidant and anti-inflammatory properties), as well as the potential to reduce our risk of chronic disease (e.g. age-related macular degeneration or Alzheimer's disease). However, not all members of the general public can or want to consume nutritional supplements (e.g. due to the cost of the supplements, or for personal reasons such as the presence of bovine gelatine which precludes the consumption of certain supplements by vegetarian or vegan groups). Consequently, focus is being placed on developing foods (such as dairy products) that are fortified with these nutrients to positively impact human health and function.

We believe that the nutritional content of the human diet can be improved by developing a nutritionally superior or "fortified" dairy product for the general population. We suggest that using dairy as a vehicle for carotenoids will enhance the delivery of these nutrients into the body.

The purpose of this project is to improve the nutritional content of the human diet by developing a yoghurt fortified with carotenoids for the general population.

Who can participate?
In order to take part in this research you must meet the following eligibility criteria:
-Aged 18-64 years.
-Not consumed any carotenoid food supplements in the last 3 months.
-No dairy or fish allergy.

-Never diagnosed with a form of cognitive impairment (e.g. Alzheimer's disease), stroke, or eye disease (e.g. glaucoma) by a medical professional.

What does the study involve?
FortiXan is a single-blind, placebo-controlled, 4-week nutritional intervention trial. Participants will be randomly allocated into one of three groups:
Group 1 (20 people) will consume one yoghurt per day that has been fortified with an emulsion of lutein combined with fatty acids (~14.5mg lutein and ~0.5mg zeaxanthin).
Group 2 (20 people) will consume one yoghurt per day that has been fortified with an emulsion of lutein combined with acetates (~14.5mg lutein and ~0.5mg zeaxanthin).
Group 3 (20 people) will consume one yoghurt per day containing no active ingredients. This is known as a placebo.

The yogurts that we are going to test in the human trial have the same amount of lutein (~15 mg combined per yogurt). The difference between them is that one has the lutein protected by fatty acids and the other has the lutein protected by acetates (a compound typically found in salt form).

Each group will be asked to consume one 100g pot of yoghurt per day for 4 weeks. Yoghurts can be eaten at any time of the day, on their own or as part of a meal (e.g. breakfast). The yoghurt pots should be stored in the fridge.

This research is a single-blind study. This mean that the Researcher will know who is consuming the fortified yoghurts and who is consuming the placebo. However, the research participants will not know who is consuming the fortified yoghurts and who is consuming the placebo. Yoghurts from all three groups will look and taste the same.

As part of this research study you will be asked to:
-Attend the Nutrition Research Centre Ireland located at Carriganore House at the West Campus of Waterford Institute of Technology on 3 occasions over a 4-week period. Two appointments (first and last visit) will last approx. 30 minutes and one appointment (the middle visit) will last 5-10 minutes.
-Consume 1 (100g) pot of yogurt per day for a total of 4 weeks.

The first and final study visit at the Research Centre will involve:
-Providing a blood sample (2 test tubes in total). This will be obtained by a trained Researcher to measure the nutrients (xanthophyll carotenoids lutein, zeaxanthin, meso-zeaxanthin) in your blood. The blood is the means by which the dietary nutrients are transported around the body. You do not need to fast for this blood sample. The blood sample will also be used to measure total antioxidant capacity and inflammatory markers (cytokines IL-6 and IL-1β, and TNF-α). While the carotenoid meso-zeaxanthin is not contained in the fortified yoghurt, it measurement in blood is required in order to accurately measure zeaxanthin concentrations in blood.
-A non-invasive, hand-held device will be used to measure carotenoid levels in human tissue at the skin surface (at a specific point on the palm of your hand).
Contact information (full name and contact telephone number) will be recorded in order to arrange study visit appointments.
-Demographic information (sex, month of birth, year of birth, education level).
Health and lifestyle information (smoking status, alcohol intake, dietary intake of carotenoids and dairy, height, and weight.
-Complete a COVID-19 screening questionnaire (via telephone) 1 day prior to your study visit. Wear a fack mask during your study visit.

The second (middle) study visit at the Research Centre will involve providing a blood sample (2 test tubes in total). You will also collect your additional supplies of your assigned yoghurt.

At the end of the 4-week study period you will be asked to return to the Research Centre where the measurements described above will be repeated.

What are the possible benefits and risks of participating?
Benefits
There is no direct benefit from participating in this study. However, we may learn new information from this study that could help in developing a fortified yoghurt suitable for the general population. At the end of the study, you will be given feedback and gain knowledge on your carotenoid status.

Risks
Following blood extraction (i.e. obtaining the blood sample), there is a risk of bruising and infection at the site of blood extraction. In order to minimise infection risk, the site of blood extraction will be cleaned using antiseptic wipes and single-use blood sampling materials (e.g. needles, test tubes) will be used. All blood sampling materials will be disposed of correctly (i.e. in a hazard waste bin). In order to minimise bruising, you will be asked to apply firm pressure to the extraction site once the needle has been removed. The research can provide assistance if required.

The ingredients of the supplements in this trial have been extensively studied and are deemed safe to consume.

Participation in this trial is not a substitute for any standard medical care and is for research purposes only.

Where is the study run from?
Carriganore House (located in the West Campus of Waterford Institute of Technology, Waterford, X91 Y236, Ireland)

When is the study starting and how long is it expected to run for?
March 2021 to December 2022

Who is funding the study?
The FortiXan (Fortification with Xanthophylls) project is funded by Science Foundation Ireland (SFI) and the Department of Agriculture, Food and the Marine on behalf of the Government of Ireland (grant #16/RC/3835-VistaMilk). Industry partners supporting this research include the Howard Foundation UK (a registered UK charity) and Industrial Orgánica (a company that commercialises carotenoids as raw materials for manufacturing food supplements).

Who is the main contact?
Dr Alfonso Prado-Cabrero (Research Fellow and Senior Scientist), aprado-cabrero@wit.ie

Study website
https://www.cognitoforms.com/NutritionResearchCentreIreland/FortificationWithXanthophyllsFortiXanTrial

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
grant #16/RC/3835-VistaMilk

Study information

Scientific Title
Fortification with Xanthophylls trial

Acronym
FortiXan

Study objectives
To improve the nutritional content of the human diet by developing and testing the effect of a dairy product fortified with carotenoids in a nutritional intervention trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approval pending, Waterford Institute of Technology Research Ethics Committee (Professor John Wells, Research Ethics Committee, C/O Graduate Studies Office, R11 The Court Yard, Cork Road Campus, SETU Waterford, Ireland; +353 51 302609; Ethics.WD@setu.ie), ref: WIT2021REC020

Study design
Single-centre single-blind placebo-controlled interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Improve the nutritional quality of the human diet in order to prevent and/or reduce the risk of chronic diseases (e.g. Alzheimer's disease, macular degeneration).

Interventions
Random allocation sequencing will be performed by the study statistician. Participants will be randomly allocated between two active and one placebo intervention groups and a 5% level of significance will be chosen (i.e. 95% confidence level). Participants will be randomly allocated into one of three groups:

Group 1 (20 people) will consume one yoghurt per day that has been fortified with an emulsion of the carotenoid lutein combined with fatty acids (~14.5mg lutein and ~0.5mg zeaxanthin).

Group 2 (20 people) will consume one yoghurt per day that has been fortified with an emulsion of lutein combined with acetates (~14.5mg lutein and ~0.5mg zeaxanthin).

Group 3 (17 people) will consume one yoghurt per day containing no active ingredients (i.e. a placebo).

Each group will be asked to consume one 100g pot of yoghurt per day for 4 weeks. The active yogurts being tested in the will trial have the same amount of lutein and zeaxanthin (~15 mg combined per yogurt). The difference between them is that one has the lutein protected by fatty acids and the other has the lutein protected by acetates (a compound typically found in salt form).

Intervention Type

Supplement

Primary outcome measure
Serum carotenoid concentrations (umol/L) of lutein, zeaxanthin and meso-zeaxanthin will be measured in blood at baseline, 2 weeks and 4 weeks, and quantified using high-performance liquid chromatography. Of note, while meso-zeaxanthin is not contained in the fortified yoghurt, its quantification is required as part of the HPLC methodology in order to determine zeaxanthin levels in blood.

Secondary outcome measures
1. Tissue carotenoid concentrations measured at baseline and 4 weeks using the Pharmanex BioPhotonic Scanner.
2. Inflammatory cytokines (IL-6, IL-1β, and TNF-a) measured measured in blood at baseline, 2 weeks and 4 weeks and quantified using solid-phase sandwich enzyme-linked immunosorbent assay (ELISA).
3. Total antioxidant capacity measured in blood at baseline, 2 weeks and 4 weeks using colorimetric microplate assay.

Overall study start date
04/03/2021

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Aged 18 - 64 years.
2. Not consumed any carotenoid food supplements in the last 3 months.
3. No dairy or fish allergy.
4. Never diagnosed with a form of cognitive impairment (e.g. Alzheimer's disease), stroke, or eye disease (e.g. glaucoma) by a medical professional.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Key exclusion criteria

1. Under 18 years of age or older than 65 years.
2. Has consumed regularly a carotenoid food supplements in the last 3 months.
3. Has an allergy to dairy or fish.
4. Has been diagnosed with a form of cognitive impairment (e.g. Alzheimer's disease), stroke, or eye disease (e.g. glaucoma) by a medical professional.

Date of first enrolment
14/02/2022

Date of final enrolment
31/08/2022

Locations

Countries of recruitment
Ireland

Study participating centre
VistaMilk Science Foundation Ireland Research Centre
Teagasc Moorepark
Fermoy
Cork
Ireland
P61 C996

Study participating centre
Nutrition Research Centre Ireland
Carriganore House
Waterford Institute of Technology West Campus
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Sponsor information

Organisation
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Sponsor type
Research organisation

Website
https://www.vistamilk.ie

Funder(s)

Funder type
Government

Funder Name
Science Foundation Ireland

Alternative Name(s)
SFI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

Funder Name
Department of Agriculture, Food and the Marine, Ireland

Alternative Name(s)
An Roinn Talmhaíochta, Bia agus Mara, An Roinn Talmhaiochta Bia agus Mara, Department of Agriculture, Food and the Marine, agriculture_ie, Department of Agriculture, Food and the Marine (Ireland), DAFM

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Ireland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/11/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon written request from bonafide research scientists to Dr Alfonso Prado-Cabrero <aprado-cabrero@wit.ie> in the format of a pseudonymised statistical database (Statistical Package for the Social Sciences programme) of quantitative data following peer-review publication of the main findings of the trial (estimated to be Feb 28th, 2023).

IPD sharing plan summary
Available on request