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A clinical trial to investigate how the DailyColors (TM) dietary supplement affects markers of health in older adults

Submission date
18/11/2024

Recruitment status
No longer recruiting

Registration date
20/11/2024

Overall study status
Completed

Last Edited
20/11/2024

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
The Mediterranean diet is known to be linked to better health, including brain health. This is thought to be due to high levels of polyphenols in these foods, particularly in fruit and vegetables. Taking supplements of key nutrients has been suggested as a way of supporting healthy ageing and protecting brain health since many adults do not eat enough of these foods in their normal diet. This study investigates the impact of a new supplement, DailyColors™ which combines extracts from polyphenol-rich foods to see if there is an impact on key indicators of health in people at risk of poor health in older age.

Who can participate?
Adults aged 50 years and over with a Body Mass Index of 25 kg/m2 and above, who are participants in the PROTECT-UK ageing cohort online platform

What does the study involve?
All participants will receive tablets in the post containing either a placebo, low dose or high dose of DailyColors™. They will take two tablets twice a day for 60 days. They will also complete online assessments of cognition and health on the PROTECT-UK platform. A sub-group of 45 participants will be invited to attend two clinics (at the start and after 60 days) to provide a blood sample and complete physiological measures (height, weight and blood pressure).

What are the possible benefits and risks of participating?
Possible benefits include any potential benefit from the supplement although these are not known. Possible risks are low but may include an adverse reaction to the supplement, or discomfort following blood sampling for the sub-group.

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

When is the study starting and how long is it expected to run for?
July 2023 to January 2024

Who is funding the study?
DailyColors™ Health Inc.

Who is the main contact?
Prof. Anne Corbett, A.M.J.Corbett@exeter.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
124914

Study information

Scientific Title
Impact of the DailyColorsTM phytonutrient supplement on health markers in older adults: an exploratory mechanistic clinical trial

Study objectives
The DailyColors(TM) phytonutrient supplement will confer indications of benefit to cognition and physiological markers of health, and will elicit impacts on inflammatory pathways as a mechanism of benefit

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/09/2023, University of Exeter Public Health & Sports Science REC (University of Exeter Medical School, Exeter, EX1 2LU, United Kingdom; +44 (0)1392 726621; shs-ethics-admin@exeter.ac.uk), ref: 2929219

Primary study design
Interventional

Study design
60-day three-arm exploratory mechanistic placebo-controlled double-blind online exploratory mechanistic randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Adults aged 50 years and above with a BMI of 25 kg/m2 or above

Interventions
Minimisation randomisation using a validated randomised software module embedded in the PROTECT platform.

Participants will be randomised into three treatment groups:
1. DailyColors (TM) phytonutrient dietary supplement High Dose (2000 mg/day) every day for 60 days
2. DailyColors (TM) dietary supplement Low Dose (750 mg/day) every day for 60 days
3. Placebo (inert packing ingredients) every day for 60 days

The DailyColors(TM) supplement is a proprietary blend of freeze-dried powders and extracts from foodstuffs found in the Mediterranean diet. Active ingredients were packed into microcrystalline cellulose capsules containing additional inert packing ingredients of Natural Rice Concentrate (NuFlow) and Natural Rice Extract (MuMag) in quantities to ensure the correct dose.

Intervention Type
Supplement

Primary outcome(s)
Cognition as measured by the FLAME computerised cognitive test system, as described below:
1. Cognition will be assessed at baseline and 60 days on the PROTECT platform within the DailyColorsTM study bespoke study area. Cognition will be assessed using the FLAME cognitive test system which involves eight cognitive tests and takes up to 45 minutes to complete. They can be completed on either a computer with a keyboard and mouse or a touchscreen device. Participants will be encouraged to complete the tests at the same time of day on each test occasion. A video explaining the tests will be shown prior to the completion of the tests. The tests are presented in a set sequence according to the paradigm validated in the published FLAME cognitive composite measure which has proven sensitivity for detecting cognitive status and change over time. The tests are:
2. Picture Recognition Stage One: A series of 20 pictures of everyday scenes and objects is presented on the screen, at the rate of one picture every three seconds, for the participant to remember. The participant is instructed that the pictures will all be reshown later mixed with very similar ones.
3. SelfOrdered Search (SOS) task assessing spatial working memory: spatial working memory is measured through this widely used test. Participants search a series of on-screen boxes to find a hidden symbol. Once found, participants search for the symbol again, remembering that the symbol will never be hidden in the same box twice. The symbol is hidden in every box once per level. After successfully completing a level, a new level opens with more boxes to search than the previous level. The outcome measure is the average number of boxes in the successfully completed trials. Participants are allowed three errors before the test terminates.

4. Paired Associate Learning (PAL) task assessing visual episodic memory: verbal short-term memory is measured through the paired associates learning test, which is widely used in the assessment of cognitive deterioration in AD. Participants are shown objects, one per “window” in a grid. Then they see the series of objects, one at a time in a random order, and select the correct “window” where the object had previously appeared. This version uses a ratchet-style approach, each successful trial is followed by one with more objects to recall and each unsuccessful trial is followed by the same number of objects as in the unsuccessful attempt. The outcome measure is the average number of correct object-place associations (“paired associates”) in the trials that were successfully completed. Participants are allowed three errors before the test terminates.
5. Digit Span task assessing working memory: numerical working memory is measured through a version of the “digit span” (DS) task, which has been widely cited in the neuropsychological literature and used in many commercially available brain-training devices. A series of numbers is shown to the participant who then enters the numbers in the same sequence as they appeared using a number keypad. The test uses a ratchet-style approach in which each successful trial is followed by a new sequence that is one digit longer than the last and each unsuccessful trial is followed by a new sequence that has the same number of digits as the unsuccessful trial. This allows an accurate estimate of the digit span to be made quickly. The outcome measure is the average number of digits in all successfully completed trials. Participants are allowed three errors before the test terminates.
6. Simple Reaction Time (SRT): the participant is instructed to respond using the right arrow key (keyboard) or touchscreen as quickly as possible every time a stimulus is presented in the centre of the screen. The speed of each response is recorded. The outcome measure is the speed and accuracy of response as a measure of attention. The test terminates after fifty stimuli are presented with an inter-stimulus interval which varies randomly between 1 and 3.5 seconds.
7. Digit Vigilance (DV): a target digit from 0 to 9 is randomly selected and constantly shown on the screen. Digits 0 to 9 are then presented one at a time at the rate of 150 per minute. The participant is required to respond using the right arrow key (keyboard) or touchscreen as quickly as possible every time a digit matches the target digit. The number of correct detections, the speed of the correct detections and the number of responses made in error (False Alarms) are recorded. The outcome measure is speed and accuracy of response as a measure of attention and processing speed. The test terminates after a total of 450 digits is presented, with 15 target digits in each block of 150 digits.
8. Choice Reaction Time (CRT): one of two different stimuli is randomly displayed with equal probability at a frequency between 1 and 3.5 seconds and remains visible until the participant responds. The participant is required to respond using the right/left arrow keys (keyboard) or touchscreen as quickly and accurately as possible using their left or right finger, respectively. The accuracy and speed of each response is recorded, and the outcome measure is attention and processing speed. The test terminates after 50 successive trials.
9. Picture Recognition Stage Two: The original pictures plus 20 very similar distractor pictures are presented one at a time in a counterbalanced order. Half of the original pictures are presented prior to the very similar distractor versions, and half afterwards. For each picture, the participant indicates whether it is the precise picture shown in Picture Recognition Stage One, by clicking or pressing the keyboard or touchscreen respectively using their right finger if it was shown, and their left finger if it was not shown, as quickly and accurately as possible. Each picture remains on the screen until a response is made. The accuracy and speed of each response are recorded, and the outcome measure is attention and processing speed. The test terminates after the participant gives a response for all 40 pictures.
10. Grammatical Reasoning task assessing verbal reasoning: The Baddeley Grammatical Reasoning test correlates with measures of general intelligence and involves determining the accuracy of grammatical statements about a series of pictures. The outcome measure is the total number of trials answered correctly, minus the number answered incorrectly, as a measure of

executive function. The test terminates after 90 seconds.

All measured at baseline, 30 and 60 days

Key secondary outcome(s)

Full cohort:
1. Digital outcomes of health and wellbeing: the following validated measures will be completed by the participant on the study website at baseline, 30 and 60 days:
1.1. Self-reported cognition measured by the IQCODE that is clinically validated for the detection of cognitive status
1.2. Quality of life measured by the EQ5D measure with EQ-VAS
1.3. Instrumental Activities of Daily Living measured by a modified self-reported six-item IADL
1.4. Symptoms of mood and depression, measured by the nine-item Patient Health Questionnaire (PHQ-9)
1.5. Symptoms of anxiety, measured by the seven-item Generalised Anxiety Disorder (GAD-7) scale
1.6. Sleep quality measured by the short-form Cognition Online Sleep Monitoring Scale (COSMOS)
1.7. Physical fitness: A series of questionnaires and tasks designed to give a robust measure of current physical fitness. This involves:
1.8. Video-led tasks: Participants will view a video that will lead them through three simple tests of physical fitness which are validated for use in older age groups. This involves:
1.8.1. The Chair Stand Test, in which the participant raises from sitting to standing as many times as they can within 30 seconds, and provides the number of times, how difficult they found it and whether they used their hands to stand up
1.8.2. The Timed Chair-Stand Test, in which the participant reports how long it takes for them to rise from sitting to standing ten times
1.8.3. Two-Minute Step Test, in which the participant reports how many times they can march on the spot in 2 minutes
1.9. Self-Reported Gait Velocity: Participants rank their walking speed using a tick-box selection. This is validated for self-report.
1.10. The Activities-specific-Balance-Confidence (ABC) scale: A widely used 16-item measure for measuring balance in older adults.
2. Epigenetic sampling and processing: Participants will receive two saliva sample kits in the post. One will be sent after the baseline assessment and one prior to the 60-day assessment. Participants will follow the kit instructions to provide a saliva sample at baseline and 60 days. The sample will be returned to Muhdo Inc. for processing and analysis. Kit identification will be enabled through entry of unique kit identifiers and participant date of birth in the online web portal hosted by Muhdo Inc. Samples will be processed by Muhdo Health Inc. to perform DNA analysis using a custom Illumina DNA array to analyse 1000 SNPs and a masked Epigenetic Illumina array to detect 30,000 CpG sites. Raw and interpreted data will be uploaded to the web portal and downloaded by trial coordinators at the University of Exeter for integration into the full trial database.

Sub-group of 45 participants, measured at baseline and 60 days:
1. Blood sampling and processing: Sub-group participants will attend the University of Exeter St Luke's Campus. Blood samples (up to 30 ml) will be taken by venepuncture by a highly experienced researcher who is a trained phlebotomist. This is a procedure which is routinely carried out by researchers at St Luke's. This visit will take place on a University of Exeter campus where there is 24-hour access to a first aid trained Estate Patrol Team. Serum separator vacutainers will be centrifuged for 15 min at 4°C and 4000 rpm. Serum will be aliquoted into microcentrifuge tubes (500 µl/tube) and all samples then frozen at -70 °C +/- 10 °C and stored

until analysis/end of the sample retention period.
2. Oral microbiome sampling and processing: Sub-group participants attending the University of Exeter St Luke’s Campus will provide a saliva sample for oral microbiome analysis. Participants will be provided with a sample collection tube and 10 ml of mouthwash (Scope, 15 wt% alcohol, Proctor & Gamble) for self-collection of samples. Participants will be instructed to refrain from eating or drinking in the 2 hours prior to providing the sample. They will swish the mouthwash for 30 seconds and expectorate it into a universal tube. Samples will be frozen at -70 °C +/- 10 °C and stored until analysis/end of the sample retention period. For analysis, oral bacteria genomic DNA will be extracted using a Gentra Puregene Buccal Cell Kit (Qiagen, Germantown, MD), according to the manufacturer's instructions. The sample libraries will be prepared for sequencing using the NEXTflex 16S V1-V3 Amplicon-Seq Kit (Bioo Scientific, Austin, USA) and sequenced using a paired-end 300 base pair Illumina MiSeq system as described previously (Vanhatalo et al., 2021).
3. Physiological measurements: Sub-group participants will provide measurements of their height, weight and blood pressure.

Completion date
24/01/2024

Eligibility

Key inclusion criteria
1. Aged 50 years or above
2. BMI >25 kg/m2
3. Living within 2 hours travel from Exeter
4. Already a participant in the PROTECT-UK study
5. Access to a tablet or computer with an internet connection
6. Good understanding of the English Language, sufficient to participate

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
150

Key exclusion criteria
1. Already taking part in another active interventional clinical trial
2. Vegan diet
3. Drinking more than five cups of coffee or tea per day
4. Regular consumption of anti-inflammatory medications
5. Use of dietary supplements rich in polyphenols (concentrate/freeze-dried powder of cherry, blueberry, pomegranate or cacao)
6. Current prescription of atorvastatin, simvastatin, calcium channel blocker (amlodipine, felodipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine, verapamil), warfarin, clopidogrel, ticagrelor, ciclosporin, sirolimus, tacrolimus and entocort due to contraindications of high intake of grapefruit
7. Diagnosis of dementia

Date of first enrolment
19/09/2023

Date of final enrolment
02/11/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Exeter
Heavitree Road
Exeter
United Kingdom
EX1 2LT

Sponsor information

Organisation
University of Exeter

ROR
https://ror.org/03yghzc09

Funder(s)

Funder type

Industry

Funder Name
DailyColors(TM) Health Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available on request from the PROTECT Research Group at protect.data@exeter.ac.uk

IPD sharing plan summary
Available on request