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Testing a red orange extract as a food supplement to improve antioxidant defense and quality of life in older adults

Submission date
14/09/2022

Recruitment status
No longer recruiting

Registration date
20/09/2022

Overall study status
Completed

Last Edited
07/11/2023

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Aging is a complex process that may involve progressive oxidative damage of biological molecules by oxygen radicals leading to progressive loss of functionality. On the other hand, during aging, the quality of life is decreased both in men and in women. Therefore, developing a nutritional anti-aging approach is of importance in a rapidly aging world population.

The aim of this study was to assess the effect of a food supplement (ROC™) in decreasing systemic oxidative stress and in improving the quality of life of both men (physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy /fatigue, emotional well-being, social functioning, pain, general health) and women (menopause symptoms).

Who can participate?
Older adults aged between 45 and 65 years of age

What does the study involve?
Participants will be asked to attend clinic visits at screening and after 2 and 8 weeks of product intake. During the screening visit, the medical doctor informed the participants about the trial procedure, risks, and benefits. Only participants giving their informed consent were enrolled in the study. The trial staff and the subjects fixed the date for the first visit when each subject will be asked to be fasting for blood withdrawal. The participants will then be randomly allocated to use the ROC food supplement or the placebo (dummy) product for 8 weeks. All the measurements/assessments will be carried out using minimally invasive procedures. The total duration of each visit will be 30 minutes. The study duration will be 8 weeks with an intermediate check at 2 weeks.

What are the possible benefits and risks of participating?
The potential benefits due to product use are related to a decrease of oxidative stress and to an

improvement of the quality of life both in men (physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, general health) an in women (menopause symptoms).

The product is manufactured according to the applicable national and international rules and regulations. All ingredients included in the product formula are approved for use in food/food supplements. The potential risks associated with the use of the product are related to both subjective and objective adverse events (AEs) (e.g., bloating, diarrhea, stomachache). The occurrence of AEs related to individual susceptibility to specific ingredients in the product could be related to the biological phenomenon that is not avoidable and cannot be considered as AEs due to product intake. Potential risks are assumed to be mild to moderate and are not expected to pose a risk to human health. Risks associated with the procedures involved in this study are judged as minor. All the measurements carried out will not be invasive and no side effects are expected from the measurement process except for blood withdrawal. Bleeding, bruising, lightheadedness (especially after donating blood), rash, skin irritation from tape or adhesive from an applied bandage, and soreness can be experienced after blood withdrawal.

Where is the study run from?
Complife Italia Srl (Italy)

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

Who is funding the study?
BIONAP srl (Italy)

Who is the main contact?
Dr Vincenzo Nobile (Italy)
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
VARI008_ IT0003333/2021

Study information

Scientific Title
Double-blind, randomized, placebo-controlled assessment of the antioxidant efficacy of an ingredient to be used in food supplements (ROC H clinical trial 2020)" aimed to assess the efficacy of "Red Orange Complex H"

Acronym
ROCH2020

Study objectives
The trial aims to evaluate the efficacy of the test product in decreasing oxidative stress in adults (aged 45-60 years old) subjects. The study further investigates the efficacy of the product in improving the quality of life of both men (physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, general health) and women (menopause symptoms).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/05/2021, University Ethics Committee of the University of Calabria (Comitato Etico Di Ateneo (CEA) Università della Calabria) (Via Pietro Bucci Cubo 15/D - 87036 Arcavacata di Rende (CS), Italy; +39 (0)984 496940; cea@unical.it), ref: 0023482

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Healthy ageing in older adults aged between 45 and 60 years old

Interventions
The active intervention (ROC™) was a standardized Red Orange Complex extract (ROC™, Bionap Srl, 95032 Piano Tavola Belpasso, CT, Italy) obtained from 3 different pigmented, red, Sicilian oranges (Citrus sinensis) varieties (Moro, Tarocco, and Sanguinello); while the placebo intervention was maltodextrin. Both the active and the placebo products were used as follows: one capsule per day intake at breakfast for 8 weeks.
Half of the test subjects were randomized to receive the test product and half of the test subjects were randomized to receive the placebo product. A restricted randomization list was created using PASS 2008 (PASS, LLC. Kaysville, UT, USA) statistical software running on Windows Server 2008 R2 Standard SP1 64-bit Edition (Microsoft, USA) by a biostatistician and stored in a

safe place. The randomization sequence was stratified using “Efron’s biased coin” algorithm with a 1:1 allocation ratio. The allocation sequence was concealed from the in-site study director in sequentially numbered, opaque, and sealed envelopes, reporting the unblinded treatment allocation (based on the subject entry number in the study). The A4 sheet reporting the unblinded treatment was folded to render the envelope impermeable to intense light. A masked allocation sequence was prepared for the staff delivering the intervention based on the subject entry number in the study.

Intervention Type
Supplement

Primary outcome(s)
Systemic antioxidants pool assessed by the following measures at baseline and after 2 and 8 weeks of product intake:
1. The concentration of glutathione in erythrocytes measured using GSH+GSSG/GSH Assay colorimetric Kit from Abcam (ref. no. ab239709)
2. d-ROMS hematic concentration measured using a FRAS 5 device (H&D srl, Parma, Italy)

Key secondary outcome(s)
Measures assessed at baseline and after 2 and 8 weeks of product intake:
1. Anti-inflammatory activity determined by TNF-alpha levels measured using sandwich ELISA from Abcam (ref. no. ab46087)
2. Quality of life in male subjects measured using the Short Form quality of life (SF-36 QoL) questionnaire
3. Menopausal symptoms in female subjects measured using the Menopause Rating Scale (MRS)
4. Safety of use by analysis of blood and urine parameters measured using the current protocol of accredited medical analysis laboratory

Completion date
31/03/2022

Eligibility

Key inclusion criteria
1. Men (50%) and women (50%) aged 45-60 years old
2. Subjects with menopausal symptoms (only for women)
3. Subjects naïve to treatment and food supplements that can interfere with the study treatment for the previous 1 month
4. Not used topical products/food supplements with similar effects to the product being tested (antioxidant) during the entire study period
5. Subjects registered with health social security or health social insurance
6. Subjects reading, understanding and signed approval of the informative consent
7. Not vegetarian
8. Subjects who will continue their normal lifestyle
9. Healthy subjects without clinical illness diagnosed with relevant diseases of the gastrointestinal system or visceral motility
10. Not pregnant
11. Non-smokers
12. Subjects available and willing to follow the procedures of the study protocol
13. Subjects able to understand the language used in the investigation centre and the information given

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
60

Key exclusion criteria
1. Subjects who do not fit the inclusion criteria
2. Subjects <45 and >60 years old
3. Clinical history of relevant present disorders or administration of drugs/food supplements that can potentially interfere with the treatment under study
4. Lack of compliance defined as not using the correct dose or placebo for >1 week, and the inability to give informed consent
5. Subjects who have changed their diet significantly or have been placed on weight reduction products
6. Smokers, obese subjects
7. Subjects changing their eating habits within the 2 weeks previous to the screening
8. Pregnancy or subjects planning a pregnancy
9. Breastfeeding
10. Subjects with a history of drug, alcohol, and other substance abuse
11. Subjects planning to change their lifestyle or physical activity
12. Known food intolerance or food allergy
13. Subjects involved in a clinical or food study within the previous month
14. Subjects who have unstable medical diseases (cardiac arrhythmias or ischemia, uncontrolled hypertension and hypotension, diabetes mellitus, kidney failure)
15. Subjects with a history of paralysis or cerebral vascular accident
16. Subjects with active cancers or on chemotherapy
17. Subjects who have been under diuretics for the previous one months
18. Other factors that limit their ability to cooperate during the study
19. Subjects deprived of freedom by administrative or legal decision or under guardianship
20. Subjects not able to be contacted in case of emergency
21. Subjects planning a hospitalisation during the study

Date of first enrolment
07/06/2021

Date of final enrolment
25/02/2022

Locations

Countries of recruitment
Italy

Study participating centre
Complife Italia Srl
Via Monsignor Angelini, 21
San Martino Siccomario (PV)
Italy
27028

Sponsor information

Organisation
BIONAP srl

Funder(s)

Funder type
Industry

Funder Name
BIONAP srl

Results and Publications

Individual participant data (IPD) sharing plan
Raw data will be stored on Complife servers. A backup copy of the raw data will be also in a cloud-based backup server. Tables containing the raw data (output of the measurements) will be also included in the study report and shared with the study sponsor by a pdf file electronically signed. The raw data will be stored for a minimum period of 10 years on Complife servers. In the raw data tables, subjects are identified by a means of a code generated by the Complife volunteer's management software. The code is composed of a letter, four digits, and a letter. Access to the study raw data is allowed only to the study director and the person designated by him to elaborate on the raw data. Elaboration of the raw data includes descriptive statistics (mean and standard error) and inferential analysis (data normality and statistical test).

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/10/2022	07/11/2023	Yes	No