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Efficacy of a food supplement in protecting the skin from sun and aging

Submission date
09/05/2022

Recruitment status
No longer recruiting

Registration date
10/05/2022

Overall study status
Completed

Last Edited
13/06/2023

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
Exposure to ultraviolet (UV)-B light elicits an inflammatory response in the skin, resulting in erythema (reddening) and increased skin blood flow (also known as UV induced erythema or sun burn)
The aim of this study was to assess the efficacy of a food supplement (ROC™) in improving the skin response to sun exposure and its antiaging effect.

Who can participate?
Patients aged 35 to 65 years with mild to moderate skin aging signs including dark spots.

What does the study involve?
Participants were asked to attend clinic visits at screening and after 14 and 56 days of product intake. At each visit, participants were asked to come to the study facilities on two consecutive days. During the screening visit, the dermatologist 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 then the date for the first visit. During the first visit, a small area on the back was exposed to a series of UV doses to determine the minimal erythema dose (MED). After the UV exposure participants were asked to come back to the trial facility 20±4 hours after the UV exposure to read the MED. The participants were then randomly allocated to use the ROC™ food supplement or the placebo (dummy) product for 56 days. All the measurements/assessments were carried out using minimally invasive procedures. The total duration of each visit was 30 minutes. The study duration was 56 weeks with an intermediate check at 14, 15*, 16*, 17*, and 56 days.
* only to measure the UV-induced skin redness after 14 days of product intake.

What are the possible benefits and risks of participating?
The potential benefits due to product use are related to photoprotective action, a decrease in the UV-induced skin erythema reaction), and a decrease in skin aging signs.
The product is manufactured according to the applicable national and international rules and regulations. All ingredients included in the product formula are approved for their 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, stomach ache). 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 from 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 are not invasive and no skin side effects are expected from the measurement process except for MED assessment. An erythema reaction is foreseen for the MED assessment procedure but, usually, this reaction disappears in a short time period until its disappearance.

Where is the study run from?
Complife Italia Srl (Italy)
Complife (Beijing) testing technology Co. Ltd.

When is the study starting and how long is it expected to run for?
July 2020 to April 2021

Who is funding the study?
BIONAP srl (Italy)

Who is the main contact?
Dr Vincenzo Nobile
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
H.E.HU.AC.NAA00.100.23.00_IT0000822/2020

Study information

Scientific Title
Photoprotective and antiaging effect of a standardized red orange (Citrus sinensis (L.) Osbeck) extract in Asian and Caucasian subjects: a randomized, double blind, controlled study

Acronym
ROCH_Sun

Study objectives
The trial was aimed to assess the efficacy of an ingredient (Red Orange Complex, ROC™), for food supplements use, in decreasing the UV-induced erythema reaction before and after 56 days product intake period. The primary outcome measure was the minimal erythema dose measurement and the instrumental measurement of the UV-induced skin redness.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/07/2020, Comitato etico indipendente per le indagini cliniche non farmacologiche (Via XX Settembre 30/4 - 16121 Genova, Italy; +39 (0)10 5454842; ssinf@messaggipec.it), ref: 2020/07

Study design
Multicenter stratified randomized double-blind placebo-controlled study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mild-to-moderate skin aging

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 56 days.

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)
UV-induced erythema reaction using instrumental measurement of skin redness at baseline and after 14, 15, 16, 17 and 56 days of product intake

Key secondary outcome(s))
Measured at baseline and after 14 and 56 days of product intake:
1. Skin moisturization (measured by means of Cor-neometer® CM 825)
2. Skin elasticity (measured by means of Cutometer® MPA 580)
3. Transepidermal water loss (measured by means of Tewameter® TM 300)
4. Total skin antioxidant capacity (FRAP assay)
5. Skin lipoperoxides content (MDA assay)
6. Intensity of melanin staining (colorimetric method)
7. Skin radiance (colorimetric method)
8. Wrinkle depth, length, area and wrinkle count (skin profilometry by structured light 3D scanner, and clinical scoring)

Completion date
21/04/2021

Eligibility

Key inclusion criteria
1. Female and male healthy subjects (between 30-50% male and 50-70% female)
2. 35 ≤ age ≤ 65 years old
3. 40% Caucasian (skin phototype* I to III) and 60% Asian (skin phototype* III to V) ethnicity
4. Mild to moderate skin aging sign including dark spots (grade 2-4; Skin Aging Atlas by Bazin R.)
5. Registration with health social security or health social insurance (if required by national regulations)
6. Promise to not use during all the study period topic products/food supplements with similar effect to that one of the product to be tested (antioxidant)
7. Commitment to sign the informed consent form (ICF)
8. Truthfulness of the personal information declared to the Investigator
9. Ability to understand the language used in the investigation centre and the information given
10. No recent participation in any other similar study
11. No sun exposure (both natural and artificial) for at least two months before study start,
12. Absence of sunburn, suntan, scars or other active dermal lesions on the area selected for test purposes
13. Color uniformity of the test area (without nevi, blemishes or solar lentigo and without hair)
14. Promise to not change the normal daily routine, effective contraceptive therapy
15. Ability to comply with the protocol and follow protocol’s constraints and specific requirements

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
110

Key exclusion criteria
1. Breastfeeding, pregnancy (or unwillingness to take necessary precautions to avoid pregnancy during the study and for at least 3 months before the inclusion visit [for women of childbearing potential]
2. Staring or changing oestrogen-progesterone contraception or hormonal treatment, within the 3 months prior to the study or foreseeing it for the duration of the study
3. Allergies or sensitivity to cosmetic products, toiletries, sunscreens, and/or topical drugs
4. Dermatological problems in the test area
5. Pharmacological treatments (both locally or systemically)
6. Positive anamnesis for atopy (allergic hypersensitivity affecting parts of the body not in direct contact with the allergen)
7. Use of self-tanning products for at least one month before study start
8. Habit to use tanning beds,
9. Medication with photosensitizing potential, drugs, and/or food supplements able to induce skin coloring, corticoids, currently or during the month before the study start
10. Participation in another clinical trial within the last two weeks prior to the inclusion visit and taking part or planning to participate to another clinical trial during the study in the same or another investigation center
11. Deprivation of freedom by administrative or legal decision or under guardianship
12. Unavailability to be contacted in case of emergency
13. Admission in a sanitary or social facility
14. Planning a hospitalization during the study
15. Impaired immune system due to immunosuppressive diseases, or use of immunosuppressive medication
16. Acute, chronic or progressive illness liable to interfere with the study data or considered by the Investigator hazardous for the subject or incompatible with the study requirements
17. History of severe reactions from exposure to sunlight (i.e., polymorphous light eruption)
18. Long-treatment or intending to have one, in particular with aspirin, products containing aspirin, corticoids, beta blockers (including eye drops), immuno-suppressive and/or desensitization drugs or under any treatment considered by the Investigator liable to interfere with the study data or incompatible with the study requirements
19. Vaccination within the 3 weeks prior to the study or intending to be vaccinated during the study
20. Any surgery, chemical or physical treatment on the experimental area within the 12 months prior to the study or foreseeing it for the duration of the study
21. Personal history of atopic dermatitis, urticaria or severe skin reaction to cosmetics, drugs or domestic products or confirmed contact dermatitis or food allergy
22. Artificial UV exposure or excessive exposure to natural sunlight or within the 2 weeks prior

to the study or foreseeing UV exposures for the duration of the study (at Investigator’s judgment)

Date of first enrolment
01/09/2020

Date of final enrolment
26/02/2021

Locations

Countries of recruitment
China

Italy

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

Study participating centre
Complife (Beijing) testing technology Co. Ltd.
Beizhan North Street N.17, Room 902
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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 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		27/05/2022	13/06/2023	Yes	No