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Assessment of the efficacy of flavonoid complex supplementation on improvement of leg discomfort: a double-blind, randomized, placebo-controlled clinical study

Submission date
10/01/2025

Recruitment status
No longer recruiting

Registration date
14/01/2025

Overall study status
Completed

Last Edited
13/01/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Tired and heavy legs are a common complaint associated with both lifestyle factors and chronic venous insufficiency (CVI, when the leg veins don't allow blood to flow back up to the heart). Nutraceuticals and compounds of natural origin (such as flavonoids) could improve blood flow and circulation. Among these, diosmin is known to improve vein health and related disorders such as CVI and haemorrhoids. The aim of this study is to assess the effectiveness of flavonoid complex supplementation on the improvement of leg discomfort.

Who can participate?
People aged 18 to 60 years experiencing leg discomfort (i.e. heavy and tired legs) and telangiectasias (also known as spider veins)

What does the study involve?
Participants are randomly allocated to take a food supplement containing a formulated flavonoid complex (diosmin and other flavonoids commonly found in citrus fruits) or a placebo over a period of 56 days.

What are the possible benefits and risks of participating?
The supplement is usually without risk for the user and can be considered safe. The possible benefits are improvement of leg discomfort due to poor circulation (such as heavy and tired legs as well as telangiectasia/spider veins) and improvement of quality of life.

Where is the study run from?
Comlife Italia s.r.l., San Martino Siccomario (Pavia) (Italy)

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

Who is funding the study?
Giellepi S.p.A. (Italy)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
H.E.HU.HV.NHE00.060.02.00_IT0006501/22

Study information

Scientific Title
Efficacy of a diosmin-based dietary supplement on signs of telangiectasia improvement

Study objectives
Investigational product is expected to improve telangectasia severity and appearance.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/02/2023, Comitato Etico Indipendente per le indagini Cliniche Non Farmacologiche (Via XX Settembre 30/4, Genova, 16121, Italy; +39 (0)105454842; a. scudieri@studinonfarmacologici.it), ref: Rif. 2023/01

Study design
Double-blind randomized placebo-controlled monocentric interventional clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Quality of life

Participant information sheet
Not applicable

Health condition(s) or problem(s) studied
Healthy adult subjects with leg discomfort (tiredness and heaviness) and telangiectasia (CEAP classification: 0-1)

Interventions
Participants are randomized (1:1) to either the active or the placebo group using a computer-generated randomization list (PASS 11, version 11.0.8, PASS, LLC. Kaysville, UT, USA).

Treatment consists of one tablet per day of dietary supplement (µsmin plus) or placebo, orally, for 56 consecutive days. Each table of verum contains 450 mg of diosmin.

Intervention Type
Supplement

Primary outcome measure
Leg discomfort (including tired and heavy legs) measured using visual analogue score (VAS) at each visit (baseline, day 14, day 28, day 56)

Secondary outcome measures
1. Appearence of telangiectsasia assessed by a dermatologist using an arbitrary scale where 0 indicates absence, 1 very mild, 2 mild, 3 moderate, and 4 severe. This is assessed at each visit (baseline, day 14, day 28, day 56)
2. Blood flow rate is measured using a laser doppler (PeriFlux 6000, Perimed Italia Srl, Cuggiono, Milan, Italy) at each visit (baseline, day 14, day 28, day 56)
3. Skin color, which is related to the hemoglobin content in the superficial microvessels, is measured using a colorimeter (Mexameter® MX18, Courage + Khazaka electronic GmbH, Köln, Germany) at each visit (baseline, day 14, day 28, day 56)
4. Quality of life is assessed using the CIVQ20 questionnaire at baseline and at the end of the study (day 56)
5. The perceived efficacy (as perceived by each participant) is assessed using a 5-point scale (strongly disagree or not satisfied at all, disagree or not satisfied, neither disagree nor agree or neither dissatisfied nor satisfied, agree or satisfied, completely agree or very satisfied) at baseline and at the end of the study (day 56)

Overall study start date
09/01/2023

Completion date
14/03/2024

Eligibility

Key inclusion criteria
1. Male and female, adult subjects (18-60 years old included)
2. Healthy subject with BMI <30 kg/m2
3. Subjects with healthy skin
4. Subject presenting telangiectasia at the level of at least one leg and perceiving one or more of the following discomforts: tired legs, heavy legs, swollen legs, leg pain, cramping, itching or tingling in the calves
5. Subjects having signed a written Informed Consent form (ICF) for his/her participation in the

study and a photograph authorization
6. Subject able to understand the language used in the investigation center and the information given
7. Subject able to comply with the protocol and follow protocol's constraints and specific requirements
8. For women of childbearing potential: committing to use effective contraceptive method for at least 3 months before the beginning of the study and throughout the study
9. Subject who agrees not to have any body care procedure done during the study at the level of the legs as well as systemic therapy able to affect the blood circulation
10. Subject who agrees not to expose himself/herself to the sun or UV rays during this study and willing to follow recommendations for photoprotection (use of his/her usual sunscreen product if needed).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
122

Total final enrolment
122

Key exclusion criteria
1. Subject having participated in another clinical trial within 30 days before the inclusion visit and for a longer period if required in the Investigator's opinion
2. Subject taking part or planning to participate in another clinical trial during the study in the same or another investigation centre
3. Subject consuming blood flow-enhancing supplements (e.g. citrulline, arginine, beetroot powder) or functional drinks (e.g. pomegranate or beetroot juice) within 1 month prior to participation
4. Breastfeeding or pregnant (for the women of childbearing potential)
5. Subject deprived of freedom by administrative or legal decision or under guardianship
6. Subject not able to be contacted in case of emergency
7. Subject admitted in a sanitary or social facilities
8. Subject planning a hospitalization or surgery during the study
9. Subjects presenting CVI = or > C2 grade on the ClinicalEtiologyAnatomyPathophysiology (CEAP)
10. Cutaneous pathology on the studied zone liable to interfere with the data of the study
11. 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
12. Subject having personal medical history liable to interfere with the study data for the subject or incompatible with the study requirements
13. Subject with vascular diseases different from telangectasia, diabetes, or blood disorders
14. Subject presenting lower limb edema due to cardiac, renal, or hepatic origin
15. Subjects with lower limb arterial disease
16. Subject presenting metabolic, neurological, or orthopedic problems, including traumas and prior amputation, arthritis, neuropathy, or other conditions such as recent vein surgery, or deep or superficial venous thrombosis of the lower limbs during the previous 6 months
17. Hypersensitivity to active principles contained in the tested dietary supplement
18. Smoker (≥10 cigarettes/day)
19. Concomitant or previous history of addiction to alcohol, excessive use of spices, or drug abuse
20. Exposure of the study areas to artificial UV or excessive exposure to natural sunlight within the 1 month before the inclusion visit (in the Investigator's opinion) or planning exposure during the study
21. Application of any cosmetic leave-on product on the study areas on the day of the visit.

Date of first enrolment
15/03/2023

Date of final enrolment
08/01/2024

Locations

Countries of recruitment
Italy

Study participating centre
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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Giellepi

Alternative Name(s)
Giellepi Spa, Giellepi S.p.A.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Italy

Results and Publications

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

Intention to publish date
30/01/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository on Complife servers. A backup copy of the raw data will also be on 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 in a PDF file that is electronically signed. The raw data will be stored for a minimum period of 10 years on Complife

servers. Access to the study's raw data is allowed only by 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