ISRCTN11708820 https://doi.org/10.1186/ISRCTN11708820

The beneficial effect on cardiovascular function of a food supplement based on a mixture of Mentha spicata L. extract, Amaranthus caudatus L. seed flour, flavonoids and vitamins.

Submission date
03/10/2024

Recruitment status
No longer recruiting

Registration date
28/11/2024

Overall study status
Completed

Last Edited
28/11/2024

Condition category
Other

[_] 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
Cardiovascular diseases (CVD) are the leading cause of death in Western countries. High cholesterol is a major risk factor for CVD, doubling the risk of developing these diseases. This study aims to evaluate the effectiveness of a dietary supplement containing various natural ingredients in controlling cholesterol levels in people with borderline high cholesterol.

Who can participate?
Adults aged 18 to 70 years with slightly elevated cholesterol levels (total cholesterol between 200 and 239 mg/dl and LDL cholesterol less than 159 mg/dl) who can understand and sign the informed consent.

What does the study involve?
Participants will be randomly assigned to one of three groups: one receiving a high dose of the supplement, one receiving a low dose, and one receiving a placebo. The study lasts for three months, with a 15-day period before starting the treatment where participants will follow a specific diet and keep a food diary.

What are the possible benefits and risks of participating?
There are no expected risks from participating in this study. The supplement may improve cardiovascular health, but there is no guarantee of benefit.

Where is the study run from?
The study is conducted at the COMEGEN General Practitioner's Medical Center in Naples, Italy.

When is the study starting and how long is it expected to run for?
March 2024 to January 2025

Who is funding the study?
GRICAR Chemical S.r.l. (Italy)

Who is the main contact?
For scientific inquiries, contact Prof. Maria Daglia at maria.daglia@unina.it.
For public inquiries, contact Alessandra Baldi at alessandra.baldi.alimenti@gmail.com.

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Efficacy study of a food supplement based on a mixture of Mentha spicata L. leaves extract, Amaranthus caudatus L. seed flour, flavonoids (naringin, hesperidin), and vitamins B3, B6, B9, B12, for the maintaining of physiological cardiovascular function in subjects with mildly altered cholesterol levels: a single-center, controlled, randomized, parallel-group, double-blind clinical trial with a run-in period

Acronym
GRICOL24

Study objectives
The study aimed to evaluate the efficacy of supplementation with a blend of Mentha spicata L. leaf extract (at two different dosages), Amaranthus caudatus L. seed flour, flavonoids (naringin, hesperidin), and vitamins B3, B6, B9, and B12 for maintaining normal plasma cholesterol levels in subjects with mildly altered (or borderline) cholesterol levels.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/07/2024, Ethics Committee CAMPANIA 1 (Via Mariano Semmola, 53, Naples, 80131, Italy; +39 081/17770131; comitatoetico@istitutotumori.na.it), ref: Prot n° 3/24

Study design
Interventional monocentric randomized parallel-group three arm double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Subjects with mildly altered cholesterol levels

Interventions
Here is the revised text for clarity:

The subjects recruited for this clinical study were randomly assigned to one of the following groups:

1. Group 1 (38 subjects): Subjects took one tablet of the nutritional supplement DOSE A, containing an extract from Mentha spicata L. leaves, Amaranthus caudatus L. seed flour, flavonoids (naringin, hesperidin), and vitamins B3, B6, B9, and B12.
2. Group 2 (38 subjects): Subjects took one tablet of the nutritional supplement DOSE B, containing an extract from Mentha spicata L. leaves, Amaranthus caudatus L. seed flour, flavonoids (naringin, hesperidin), and vitamins B3, B6, B9, and B12.
3. Group 3 (38 subjects): Subjects took a placebo.

The treatment lasted for 3 months. Before starting the treatment, subjects underwent a 15-day run-in period with no treatment, during which they began an isocaloric diet and completed a daily food diary.

All subjects were instructed to follow an isocaloric diet throughout the study. This diet emphasized fruits, vegetables, whole grains, low-fat dairy, fish, white meat, and vegetable oils, while reducing red meat, animal fats, salt, simple sugars, and alcohol. The dietary guidelines were based on the DASH diet, which helps control blood pressure and improve insulin resistance, hyperlipidemia, and obesity. Compliance with the diet was monitored using a food diary provided at the screening visit, which subjects brought to each visit.

The treatment consisted of COLEMIN® 100 or COLEMIN® 75 dietary supplements, containing Naringin, Hesperidin, AMASPIC® (Mentha spicata L. leaf extract, Amaranthus caudatus L. seed powder), and vitamins B3, B6, B12, and Folate. These supplements were notified to the Ministry of Health (notification numbers: 172704 for COLEMIN® 75 and 172702 for COLEMIN® 100).

To maintain the double-blind design, the three treatments were made indistinguishable, with identical packaging and dosage forms in color, shape, weight, and taste.

The randomization sequence was generated by a statistician using STATA 16 software, and the randomization list was kept hidden. Participants were randomly assigned to one of the three treatment groups (DOSE A, DOSE B, or placebo) through simple randomization. The randomization code consisted of a three-digit number as indicated in the Case Report Form (CRF).

Participants attended four visits: at the start of the run-in period (tr), at the start of the treatment period (t0), after 30 days of treatment (t1), and at the end of the treatment period (90 days) (t2). After each visit, data were recorded in the CRF by physicians.

Clinical trial design:

Tr. Screening and start of run-in (two weeks):
- Evaluation of eligibility based on inclusion and exclusion criteria
- HIV test using a combined rapid saliva test (4th generation)
- Pregnancy test for women of child-bearing age
- Cholesterol measurements
- Delivery of the food diary for the study duration
- Instructions on the isocaloric diet

T0. Start of the treatment period (Baseline):
- Collection of the food diary
- Outcome assessment: total, LDL, and HDL cholesterol, triglycerides, glycated hemoglobin, fasting glycemia, BMI, waist circumference, white blood cell count, ESR, CRP, creatinine, SGOT, and SGPT
- Randomization into the three experimental groups
- Delivery of experimental treatments for the first 30 days

T1. At 30 days of the treatment period:
- Collection of the food diary
- Collection of treatment boxes (compliance assessment)
- Outcome assessment: SGOT and SGPT
- Delivery of experimental treatments for the remaining days

T2. End of the treatment period (90 days):
- Collection of the food diary
- Collection of treatment boxes (compliance assessment)
- Outcome assessment: total, LDL, and HDL cholesterol, triglycerides, glycated hemoglobin, blood glucose, BMI, waist circumference, white blood cell count, ESR, CRP, creatinine, SGOT, and SGPT

If you need any further adjustments, feel free to let me know!

Intervention Type
Supplement

Primary outcome(s)
1. LDL cholesterol concentration is measured using a blood test at run-in, baseline (t0), and 90 days (t2) of treatment
2. Total plasma cholesterol concentration is measured using a blood test at run-in, baseline (t0), and 90 days (t2) of treatment

Key secondary outcome(s))
1. Total cholesterol (TC) is measured using a blood test at run-in (tr), baseline (t0), and 90 days (t2) of treatment
2. HDL cholesterol is measured using a blood test at baseline (t0) and 90 days (t2) of treatment
3. Triglycerides (TG) are measured using a blood test at baseline (t0) and 90 days (t2) of treatment
4. Glycated hemoglobin is measured using a blood test at baseline (t0) and 90 days (t2) of treatment
5. Blood glucose is measured using a blood test at baseline (t0) and 90 days (t2) of treatment
6. Body weight is measured using BMI (kg/m²) and abdominal circumference at baseline (t0) and 90 days (t2) of treatment

7. White blood cells are measured using a blood test at baseline (t0) and 90 days (t2) of treatment
8. Erythrocyte sedimentation rate (ESR) is measured using a blood test at baseline (t0) and 90 days (t2) of treatment
9. C-reactive protein (CRP) is measured using a blood test at baseline (t0) and 90 days (t2) of treatment
10. Serum Glutamic Oxaloacetic Transaminase (SGOT) is measured using a blood test at baseline (t0), 30 days (t1), and 90 days (t2) of treatment
11. Serum Glutamate Pyruvate Transaminase (SGPT) is measured using a blood test at baseline (t0), 30 days (t1), and 90 days (t2) of treatment
12. Creatinine is measured using a blood test at baseline (t0), 30 days (t1), and 90 days (t2) of treatment

Completion date
13/01/2025

Eligibility

Key inclusion criteria
1. Were aged between 18 and 70 years
2. Were able to understand and sign the informed consent
3. Had a negative HIV test
4. Had a negative pregnancy test
5. Had borderline total cholesterol values, between 200 and 239 mg/dL
6. Had LDL cholesterol values < 159 mg/dL
7. Were not taking and did not take any type of medication throughout the study period

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Total final enrolment
114

Key exclusion criteria

1. Age < 18 or > 70 years
2. Subjects at high risk for cardiovascular events based on 8 risk factors (sex, age, diabetes, smoking habits, systolic blood pressure, total cholesterol, HDL cholesterol, and antihypertensive treatment) according to the parameters of the Cuore Project of the Istituto Superiore di Sanità
3. On pharmacological therapy for cholesterol, including low doses
4. Use of supplements for cholesterol control, glycemia, and metabolic syndrome in the two weeks preceding recruitment
5. Pregnant women, suspected pregnancy, or planned pregnancy
6. Women in lactation
7. Blood donors in the three months preceding recruitment
8. Non-self-sufficient individuals
9. Individuals unwilling to collaborate
10. Individuals unable to attend the reference facility within the required time frame
11. Subjects deemed unsuitable by the principal investigator due to other conditions considered incompatible with enrollment and requiring pharmacological treatments
12. Subjects with acquired immunodeficiency due to HIV

Date of first enrolment
18/09/2024

Date of final enrolment
27/09/2024

Locations

Countries of recruitment
Italy

Study participating centre
COMEGEN General practitioner's medical center
Viale Maria Bakunin, 41
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Sponsor information

Organisation
GRICAR Chemical S.r.l.

Funder(s)

Funder type

Industry

Funder Name
GRICAR Chemical S.r.l.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes