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The beneficial effect on cardiovascular function of a food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid.

Submission date
14/11/2023

Recruitment status
No longer recruiting

Registration date
29/11/2023

Overall study status
Completed

Last Edited
11/09/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Cardiovascular diseases (CVD), which are the main cause of death in Western countries, have a multifactorial etiology. Age, sex, arterial hypertension, cigarette smoking habits, diabetes, and hypercholesterolemia are the most representative risk factors for CVD. The latter plays a major role in the development of atherosclerotic disease and its complications, representing, together with arterial hypertension, the risk factor with the greatest pathophysiological and prognostic impact. In fact, people with hypercholesterolemia have approximately double the risk of developing CVD compared to those with normal total cholesterol levels. Furthermore, patients with familial hypercholesterolemia have an even greater risk of developing CVD at an early age and, therefore, early diagnosis and reduction of this disease risk factor are essential to reduce cardiovascular events and premature death.
Statins are the most commonly used drug treatment to treat hypercholesterolemia. However, the limitations of such drugs are related to treatment resistance and intolerance due to adverse events leading to a lack of adherence to therapy with poor therapeutic outcomes. The most frequent adverse effects attributable to the use of statins are gastrointestinal disorders, headache, increased levels of liver enzymes in the blood, liver disorders, myalgia, myopathy, muscle cramps, rhabdomyolysis, weakness, sleep disorders, etc.
Before arriving at pharmacological therapy and based on the risk to which the subject is exposed, it is possible to modify the modifiable risk factors through lifestyle changes and the improvement of eating habits, which include a healthy and balanced diet including possible consumption of food supplements, and implementation of physical activity. Prevention is the main strategy to maintain cholesterol levels within recommended levels and reduce the incidence of developing CVD. In recent years, food supplements have acquired more and more interest from the medical profession as a strategy for maintaining cholesterol levels below the limits that define the condition of hypercholesterolemia. Food supplements intended for cholesterol control are increasingly made up of multiple bioactive ingredients, which act on different metabolic targets.
In the scientific literature, numerous studies are reported demonstrating the anti-

hypercholesterolemic activity of red yeast rice (which in turn contains monakolin K and gamma-aminobutyric acid) and gamma-oryzanol.

This study aimed to evaluate the efficacy of supplementing the diet with a food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid, in improving cardiovascular health.

Who can participate?
Subjects aged 18-70 years of either sex, who have borderline hypercholesterolemia and that are able to understand and sign the informed consent.

What does the study involve?
The subjects recruited in the present clinical study will consume a food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid, or a placebo, for 90 days, based on the randomization group.

What are the possible benefits and risks of participating?
An improvement in the clinical cardiovascular health of the subjects randomized in the food supplement group is hypothesized. However, no benefit may be achieved.
No risks are foreseen.

Where is the study run from?
Comegen, Naples (Italy)

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

Who is funding the study?
Istituto Nazionale Biostrutture e Biosistemi (Italy)

Who is the main contact?
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Protocol serial number
RPF23_01

Study information

Scientific Title
Study of the efficacy of supplementation with a mixture of red fermented rice (monacolin K), gamma-oryzanol from rice bran (Oryza sativa L.), and gamma-aminobutyric acid for the maintenance of normal cardiovascular function in subjects with mildly altered cholesterolemia: single-center, controlled, randomized, parallel-arm, double-blind clinical study with run-in period

Acronym
RPF23

Study objectives
The aim of this study was to evaluate the efficacy of the supplementation of the diet with a food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid, in improving cardiovascular health.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/06/2023, Ethics Committee of ASL Napoli1CENTRO (Via Comunale del Principe, 13 /A, Napoli, 80145, Italy; +39 (0)812544495; comitatoetico@aslnapoli1centro.it), ref: 294

Primary study design
Interventional

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

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Mild hypercholesterolemia

Interventions
The subjects recruited in the present clinical study will consume a food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid, or a placebo, for 90 days, based on the randomization group.
In particular: red yeast rice (monacolin K), gamma-oryzanol from rice bran (Oryza sativa L.), and gamma-aminobutyric acid.

The randomization sequence will be generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) and the randomization list will be kept hidden. The participants will be assigned to each of the two treatment groups (food supplement or placebo) casually and by simple randomization (1:1 allocation ratio). The randomization code will consist of a three-digit number as indicated in the respective Case Report Form (CRF).

In the clinical study, 88 participants will be enrolled and divided into two groups (44 for each group):

- Group 1: food supplement based on red yeast rice (monacolin K), gamma-oryzanol from rice bran, and gamma-aminobutyric acid.
- Group 2: placebo.

Participants will undergo four visits (screening visit = tr; baseline = t0; after 30 days of treatment = t1; after 90 days of treatment = t2) in an outpatient setting. After each clinical visit, all data are filled in the CRF by physicians.
The clinical trial design is reported below:
During the screening visit, subjects will undergo the following investigation to understand if

they meet the study participation requirements:
- Borderline hypercholesterolemia:
o 200 mg/dL < Total Cholesterol < 239 mg/dL
o LDL cholesterol < 159 mg/dL

Subsequently, all enrolled subjects will undergo the following:
- 15 days run-in period with standard diet, for all enrolled subjects.
- at t0, and t2 (at baseline, and 90 days from the start of treatment) LDL cholesterol, Total Cholesterol (TC), HDL cholesterol, triglycerides (TG), glycated hemoglobin (HbA1c), glycemia, Body Mass Index (BMI), waist circumference, leukocytes, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP).
- at t0, t1, and t2 (at baseline, 30 and 90 days from the start of treatment) liver and kidney toxicity – Glutamate Oxaloacetate Transaminase (GOT), Glutamate Pyruvate Transaminase (GPT), and creatinine.

Intervention Type
Supplement

Primary outcome(s)
Plasmatic LDL determination measured using blood sample analysis at the screening visit (tr), baseline (t0), 90 days of treatment (t2)

Key secondary outcome(s)
1. Determination of blood levels of TC, HDL cholesterol, TG measured using blood sample analysis at the screening visit (tr) –TC and HDL only, baseline (t0), 90 days of treatment (t2).
2. Determination of blood levels of HbA1c, and fasting blood glucose measured using blood sample analysis at baseline (t0), 90 days of treatment (t2).
3. BMI (kg/m²) and waist circumference (cm) measured using anthropometric measures at baseline (t0), 90 days of treatment (t2).
4. Inflammatory levels, leucocyte, ESR, CRP measured using blood sample analysis at baseline (t0), 90 days of treatment (t2).
5. Liver and kidney toxicity, blood concentration of the following biomarkers GOT, GPT, and creatinine measured using blood sample analysis at baseline (t0), 30 days of treatment (t1), 90 days of treatment (t2).

Completion date
15/02/2024

Eligibility

Key inclusion criteria
1. Subjects aged 18-70 years of both sexes;
2. Subjects able to understand and sign the informed consent;
3. 200 mg/dL < Total Cholesterol < 239 mg/dL;
4. LDL cholesterol < 159 mg/dL.

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
88

Key exclusion criteria
1. Aged < 18 and > 70 years;
2. Who have a medical history or condition that could affect the subject's safety or negatively impact the validity of the study results;
3. Pregnant or breastfeeding women;
4. With history of allergy to ingredients contained in the study treatments (dietary supplement and placebo);
5. Exposed to a high risk of cardiovascular events based on 8 risk factors (sex, age, diabetes, smoking habits, systolic blood pressure, total cholesterolemia, HDL-cholesterolemia and antihypertensive treatment);
6. Following drug therapy for cholesterol even at low doses;
7. Taking supplements to control cholesterol, blood sugar and metabolic syndrome, in the two weeks prior to recruitment;
8. Women who are pregnant, suspect pregnancy or planning pregnancy;
9. Women who are breastfeeding;
10. Blood donors in the three months prior to recruitment;
11. Non-self-sufficient individuals;
12. Who do not show a propensity to collaborate;
13. Who have difficulty getting to the reference facility within the scheduled time;
14. Who are not considered suitable by the investigators due to the presence of other pathologies considered incompatible with enrollment.

Date of first enrolment
21/09/2023

Date of final enrolment
02/10/2023

Locations

Countries of recruitment
Italy

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Sponsor information

Organisation
Istituto Nazionale Biostrutture e Biosistemi

ROR
https://ror.org/043bhwh19

Funder(s)

Funder type
Research organisation

Funder Name
Istituto Nazionale Biostrutture e Biosistemi

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed 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?
Results article		04/09/2024	11/09/2024	Yes	No