ISRCTN84281116 https://doi.org/10.1186/ISRCTN84281116

The effect of Robuvit on the healing process of non-alcoholic fatty liver disease

Submission date	**Recruitment status**	[X] Prospectively registered
20/10/2023	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
23/11/2023	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
23/11/2023	Digestive System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Non-Alcoholic Fatty Liver Disease (NAFLD) is currently seen as the most common long-term liver problem in developed countries. NAFLD is closely tied to its main causes like being overweight, having metabolic issues, and Type 2 Diabetes. NAFLD is a kind of liver problem that shows up in different forms, including a fatty liver, a more severe version called Non-Alcoholic Steatohepatitis (NASH), and liver scarring.

To deal with NAFLD, the approach involves working on the liver problem and the other health issues that often come with it, such as being overweight, high cholesterol, high blood pressure, insulin resistance, and diabetes. This includes making changes to your lifestyle like losing weight, getting more active, and sometimes taking medications. The main goal is to reduce the inflammation that's harming your liver and prevent liver scarring from getting worse.

For people with NAFLD, it's also recommended to consider non-medical treatments like dietary supplements. Some initial studies have been done with a supplement called Robuvit, which is made from certain parts of oak trees.

The goal of this research is to see what happens when people with NAFLD or a similar liver issue called MAFLD take Robuvit every day. They want to find out if it helps with the symptoms of the disease, stops the liver from getting worse, and figures out how it might help the liver heal itself. They also want to see if Robuvit can have an impact on the other problems that often come with a fatty liver, like high cholesterol, being overweight, blood sugar issues, and high blood pressure.

Who can participate?
NAFLD patients aged 20 to 75 years on the same standard treatment during the study period.

What does the study involve?
In this scientific study, we're going to look at the effects of taking Robuvit® for 12 weeks, with a dose of 300 mg per day (200 mg in the morning and 100 mg at lunch). We'll study how it impacts the symptoms of non-alcoholic fatty liver disease (NAFLD) or a similar condition called metabolically associated non-alcoholic fatty liver disease (MAFLD).

To do this, we'll gather a group of patients who meet certain criteria for the study and split them into two groups:

1. Intervention Group: They will take 300 mg of Robuvit® every day for three months (12 weeks).
2. Control Group: They will take a placebo (a dummy pill with no active ingredients) every day for three months (12 weeks).

We'll randomly decide who goes into which group using a computer program.

During the study, the patients will have check-ups with the doctor after the first 6 weeks and then again after the next 6 weeks. At these appointments, they'll answer questions about their quality of life. Also, blood samples will be taken at all three appointments. Importantly, neither the patients nor the researchers will know who is in the Robuvit® group and who's in the placebo group.

In addition to taking Robuvit® or the placebo, patients will continue with their regular medical treatment during the study. Robuvit® will be provided to the volunteers for free in capsule form. Before the study begins, after 6 weeks, and after 12 weeks of taking Robuvit® or the placebo, patients will have medical check-ups, complete quality of life questionnaires, and have their blood tested to check specific health markers.

If a patient has been taking a medication called Lagosa, they can only be included in the study one month after they've stopped taking it.

What are the possible benefits and risks of participating?
Participants who receive Robuvit® may benefit from the improvement of liver regeneration and quality of life of patients with NAFLD and MAFLD. There are no known risks to participants taking part in this study. The use of Robuvit® has been recognized as safe (GRAS certificate), and the product has received the status of Kosher and GMP (good manufacturing practice). Robuvit® is freely available in Slovakia as a nutritional supplement.

Where is the study run from?
1. Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry, Faculty of Medicine, Comenius University, Bratislava, Slovakia
2. The 3rd Internal Clinic, Faculty of Medicine, Comenius University and University Hospital, Bratislava, Slovakia

When is the study starting and how long is it expected to run for?
June 2023 to June 2026

Who is funding the study?
Horphag Research Ltd (Switzerland)

Who is the main contact?
Prof Jana Muchová, jana.muchova@fmed.uniba.sk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
V02

Study information

Scientific Title
The effect of Robuvit on the healing process of non-alcoholic fatty liver disease: a randomised controlled trial

Acronym
RobuFaL

Study objectives
The aim of this project is to find the effect of 12 weeks administration of Robuvit in a dose of 300 mg/day on disease symptoms, tissue fibrosis progression, mechanisms involved in the liver regeneration process and quality of life of patients with non-alcoholic fatty liver disease (NAFLD) or metabolically associated non-alcoholic fatty liver disease (MAFLD).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/06/2023, Ethics Committee of University Hospital Bratislava Kramáre- Academician Ladislav Dérer Hospital (Limbová 5, Bratislava, 83305, Slovakia; +4212/ 5954 2485; eticka.komisia@kr.unb.sk), ref: 23/2023

Primary study design
Interventional

Study design
Interventional double-blinded randomized placebo-controlled study

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Non-Alcoholic Fatty Liver Disease (NAFLD)

Interventions
This double-blind, randomized, placebo-controlled project will study the effect of 12 weeks administration of Robuvit in a dose of 300 mg/day (200 mg in the morning and 100 mg at lunch) on disease symptoms, tissue fibrosis progression, mechanisms involved in the liver regeneration process and quality of life of patients with non-alcoholic fatty liver disease (NAFLD) or metabolically associated non-alcoholic fatty liver disease (MAFLD).

Patients meeting the criteria for inclusion in the project will be randomly divided into two groups:
1. Intervention group - supplementation with Robuvit® in daily dose 300 mg/day during 3 months
2. Control group - supplementation with placebo in daily dose 300 mg/day during 3 months

Randomization will be performed using statistical program StatDirect. The code for assigning participants to one of the two study groups will be randomly generated by computer using block randomization. Randomization will be performed by a statistician who will not have contact with the study participants. The research team and doctors will not know the group to which the participants have been assigned. The resulting grouping code, sealed in an envelope, will be kept by the responsible solver in case of medical complications, when the code may be unblinded.

In addition to supplementation (with Robuvit® or Placebo) patients will continue in standard treatment during the course of the project. Robuvit® will be provided to volunteers free of charge in the form of capsules. Before the start (sampling 0), after 6 weeks (sampling 6) and after 12 weeks of supplementation with Robuvit® / Placebo (sampling 12), the patients will be clinically examined by an internal physician, they will fill out a questionnaire on the quality of life (SF-12) and biological material (total blood) will be collected to determine the planned parameters.

Intervention Type
Supplement

Primary outcome(s)
1. Effect on the functional parameters of the liver.
Total plasma proteins, albumin, prealbumin, ALT, AST, ALP (alkaline phosphatase), LDH, CHE, GMT, IgA, bilirubin (conjugated, non-conjugated), prothrombin, prothrombin time, total transferrin, iron, measured at certified Laboratory of Clinical Biochemistry at baseline and after 6 and 12 weeks of intervention.
2. Effect on the lipid profile and Cyt-2E1 and PON1 activities. Lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol, TAG), measured at certified Laboratory of Clinical Biochemistry at baseline and after 6 and 12 weeks of intervention. HDL and LDL subfractions measured using electrophoretic Lipoprint system at baseline and after 12 weeks of intervention. Activities of Cyt-2E1 biotransformation enzyme and PON 1 (arylesterase and lactonase) using spectrophotometric method at baseline and after 6 and 12 weeks of intervention.
3. Effect on liver steatosis and fibrosis progression measured using transient elastography at baseline and after 12 weeks of intervention.

Key secondary outcome(s)

1. Changes in basic and specific biochemical parameters (fasting glucose, total plasma proteins, blood count, uric acid, urea, a2-macroglobulin, apolipoprotein A-I,) measured at certified Laboratory of Clinical Biochemistry at baseline and after 6 and 12 weeks of intervention. Hyaluronic acid measured using ELISA at baseline and after 12 weeks of intervention.
2. Changes in glycaemic control markers (insulin, insulin resistance, leptin, adiponectin) measured at certified Laboratory of Clinical Biochemistry at baseline and after 12 weeks of intervention,
3. Changes in the level of free fatty acids in the plasma measured by gas chromatography at baseline and after 6 and 12 weeks of intervention,
4. Changes in the quality of life of patients with NAFLD evaluated by SF-12 questionnaire at baseline and after 6 and 12 weeks of intervention.

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. NAFLD patients aged 20 - 75 years on the same standard treatment during the study period. Standard treatment assumes and guarantees that patients will not take any other drugs
2. Patients willing to sign informed consent
3. Patients willing to take daily Robuvit® / Placebo and provide blood samples.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
20 Years

Upper age limit
75 Years

Sex
All

Key exclusion criteria
1. Patients under 20 or over 75 years of age.
2. Patients enrolled in other study.
3. Patients with an unstable, severe or rapidly progressing form of the disease.
4. Patients with kidney damage, infected with the HIV virus, with other serious diseases of the cardiovascular system, kidneys, gastrointestinal tract, hematopoietic system, with malignant diseases, etc.)
5. Participants who are unable / unwilling to sign an informed consent.
6. Participants who are unable / unwilling to provide samples of biological material as needed

Date of first enrolment
01/01/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
Slovakia

Study participating centre
Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry, Faculty of Medicine, Comenius University
Sasinkova 2
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Study participating centre
The 3rd Internal Clinic, Faculty of Medicine, Comenius University and University Hospital
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Sponsor information

Organisation
Horphag Research (Switzerland)

ROR
https://ror.org/003n34405

Funder(s)

Funder type
Industry

Funder Name

Horphag Research (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan
The data sets generated during and/or analysed during the current study will be available upon request from jana.muchova@fmed.uniba.sk

IPD sharing plan summary
Available on request