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Metabolism of components from a natural French oak wood extract (Robuvit®) in healthy volunteers

Submission date 03/10/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 19/11/2024	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 19/11/2024	**Condition category** Other	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Robuvit® is a standardized extract from French oak wood, containing at least 40% polyphenols, mainly ellagitannins. It offers benefits like improved vitality, stress reduction, muscle mass gain, and enhanced mood, all linked to urolithins - active metabolites produced by the gut microbiome (bacteria). The well-known urolithin A has anti-inflammatory, antioxidant, and mitophagy-promoting effects, but its behavior in the body is not well understood. Since ellagitannins are found in common foods like fruits and nuts, it’s essential to investigate how urolithins are absorbed and retained. To explore their effects after ellagitannin intake, researchers will conduct a human study analyzing metabolite concentration in blood and saliva after volunteers take Robuvit®.

Who can participate?
Healthy adults (male/female) aged 18 to 65 years

What does the study involve?
The study will be conducted in three phases. In Phase 1, the researchers will identify suitable candidates who produce urolithins after taking a 500 mg dose of Robuvit®. Participants will be asked to provide blood and saliva samples after 24 hours. Those who cannot produce urolithins will be excluded from the study.
In Phase 2 participants will first undergo a 7-day washout period, during which they must avoid foods containing ellagitannins to ensure that no urolithins remain in their system. After this period, 20-25 urolithin-producing participants will take a 500 mg dose of Robuvit®, followed by 1.5 g of blue food dye mixed into plain yoghurt 1 hour later. The time it takes for the blue dye to appear in their stool will indicate gut transit time. Serum and saliva samples will be collected at various timepoints: 0, 6, 8, 10, 12, 24, 30, 48, 54, 72, and 78 hours. After this phase, participants will have three rest days without any sampling.
In Phase 3 participants will receive a daily dose of 300 mg of Robuvit® for four consecutive days. Saliva samples will be collected according to the same schedule as in Phase 2. Blood samples will be taken at the following timepoints: 0, 6, 10, 24, 30, 48, 54, 72, and 78 hours.

What are the possible benefits and risks of participating?
Robuvit® is a natural standardized extract from French oak that positively influences vitality, activity, stress, muscle mass gain, and mood. There are no known risks to participants.

Where is the study run from?
Comenius University (Slovakia)

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

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

Who is the main contact?
RNDr. Paduchová Zuzana, PhD, zuzana.paduchova@fmed.uniba.sk

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Mrs Zuzana Paduchova

ORCID ID
https://orcid.org/0000-0002-8488-3888

Contact details
Sasinkova 2
Bratislava
Slovakia
81108
+421 (0)2 90119 411
zuzana.paduchova@fmed.uniba.sk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
QR2024-01

Study information

Scientific Title
Single intake and steady-state kinetics of ellagitannin metabolites after intake of French oak wood extract (Robuvit®) in serum and saliva – a human study

Acronym
RobuFarm

Study objectives
The goal of this study is to acquire reliable kinetic profiles for urolithins and their glucuronides in serum and saliva after a single intake of Robuvit® and under steady-state conditions.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/07/2024, Ethics Committee of Faculty of Medicine Comenius University and University Hospital in Bratislava, Old Town Hospital (Mickiewiczova 13, 81369, Bratislava, 81369, Slovakia; +421 (0)2 57290 434; michaela.vaczyova@sm.unb.sk), ref: 53/2024

Study design
Prospective interventional study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Community

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
In the 1st and 2nd phases of the study, healthy volunteers will ingest a single dose of Robuvit (500 mg) and provide blood and saliva samples. In the 3rd phase, volunteers will take a daily dose of 300 mg of Robuvit for 4 days. Robuvit is a standardized extract from the wood of the French oak, prepared in 100 mg capsules by Horphag Research Ltd. (Geneva, Switzerland).

Intervention Type
Supplement

Primary outcome measure
Urolithins kinetics after intake of a single dose of Robuvit® and under steady-state conditions analysed with a liquid chromatography system with a triple quadrupole mass spectrometer detector (LC-MS). The times of serum and saliva sampling in phase 2 will be at t = 0, 6, 8, 10, 12, 24, 30, 48, 54, 72 and 78 hours. If the blue gut transit time indicator is not detected in stool after 4 days, the measurement period may be extended by one day (to 96 or 102 hours). In phase 3, saliva sampling will be conducted as in phase 2, while serum sampling will be limited to time points t = 0, 6, 10, 24, 30, 48, 54, 72, and 78 hours.

Secondary outcome measures
1. Correlation analysis: The kinetic profiles of urolithins in serum and saliva measured using LC-MS at different timepoints (t = 0, 6, 8, 10, 12, 24, 30, 48, 54, 72 and 78 hours), and gut transit time assessed by monitoring the presence of blue color in stool after ingesting a blue food dye as a visual marker 1 hour after consuming Robuvit® (individually from hours to days)
2. The levels of urolithins in saliva and blood serum compartments measured by LC-MS at 24 hours after a single dose of Robuvit® to assess the suitability of using saliva for metabotype screening

Overall study start date
23/01/2024

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Healthy males/females between the age of 18-65 years
2. Will to adhere to dietary limitations during conduction
3. Signed informed consent

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
Both

Target number of participants
20-25 urolithin-producing participants

Total final enrolment

35

Key exclusion criteria
1. Severe/uncontrolled diseases of infectious diseases (e.g., hepatitis)
2. Volunteer cannot take or refuses to take Robuvit® for any reason
3. Age under 18 or over 65 years
4. Volunteer belongs to urolithin-nonproducing metabotype
5. Intake of antibiotics within 4 weeks prior to or during the study

Date of first enrolment
15/10/2024

Date of final enrolment
30/11/2024

Locations

Countries of recruitment
Slovakia

Study participating centre
Comenius University Bratislava
Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry
Faculty of Medicine
Sasinkova 2
Bratislava
Slovakia
81108

Sponsor information

Organisation
Horphag Research (Switzerland)

Sponsor details
71, avenue Louis Casaï
Geneva
Switzerland
CH-1216 Cointrin
+41 (0)22 710 26 26
carolina.burki@horphag.com

Sponsor type
Industry

Website
http://www.pycnogenol.com

ROR
https://ror.org/003n34405

Funder(s)

Funder type
Industry

Funder Name
Horphag Research

Results and Publications

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

Intention to publish date
02/01/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Zuzana Paduchova (zuzana.paduchova@fmed.uniba.sk)

IPD sharing plan summary
Available on request