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Effect of maritime pine bark extract, Pycnogenol, on chronic tinnitus (ringing or buzzing in the ears)

Submission date 15/02/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 03/03/2023	**Overall study status** Ongoing	
Last Edited 09/09/2024	**Condition category** Ear, Nose and Throat	

Plain English summary of protocol

Background and study aims
Tinnitus is one of the most common ear symptoms, defined as conscious awareness of sound in the absence of an external auditory stimulus. In most cases, tinnitus develops as a result of various causes (e.g. sudden hearing loss, noise trauma, ototoxic drugs, head injury or depression). It is assumed that oxidative stress plays a crucial role in the etiopathogenesis of tinnitus. Currently, no universal cure exists for patients suffering from tinnitus and the available treatment is not sufficient for their quality of life. Pycnogenol® (PYC) is natural standardised extract from pine bark and has multiple health benefits. It has strong antioxidant properties, stimulates activity of antioxidant enzymes, protects vascular endothelium, improves microcirculatory function, stimulates the production of NO by stimulating NO synthase, and others. This double-blind, randomized, placebo-controlled study aims to investigate the effect of daily use of PYC (150 mg per day) on symptoms of tinnitus, quality of life and markers of oxidative stress in patients with chronic tinnitus for 3 months.

Who can participate?
Adults aged 18 to 70 years suffering from chronic tinnitus for at least 6 months.

What does the study involve?
In the randomised, double-blind placebo-controlled study, the improvement effects of PYC (PYC-group) on the management of patients with chronic tinnitus will be compared with placebo (PL-group). Patients who meet the inclusion criteria, after initial medical investigation (complete medical history and examination, demographic and anthropometric data, audiometry, questionnaire about quality of life) will be allocated to one of the two arms of the project (PYC or PL-group) in ratio 1:1, according to a computer-generated random sequence (visit 1). Patients will be administered 150 mg PYC or Placebo for 3 months. Subsequently, patients will be examined by audiometry, to determine changes in intensity, noise and frequency of tinnitus and masking tone change, and patients will fill out a questionnaire about quality of life (visit 2). At each visit, blood samples will be taken. The randomisation will be performed by the statistician, who will have no contact with the participants. The research team and participants will be unaware of the group assignments.

What are the possible benefits and risks of participating?
Participants who receive Pycnogenol® may benefit from the reduction of the symptoms of tinnitus and improvement of their quality of life. There are no known risks to participants taking part in this study.

Where is the study run from?
1. Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry, Comenius University, Bratislava, Slovakia
2. Department of Otorhinolaryngology - Head and Neck Surgery, Faculty of Medicine and University Hospital, Comenius University Bratislava, Slovakia

When is the study starting and how long is it expected to run for?
May 2022 to December 2025

Who is funding the study?
Horphag Research Ltd, Geneva, Switzerland

Who is the main contact?
RNDr. Paduchová Zuzana, PhD.
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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
TinniPYC V.03

Study information

Scientific Title
TinniPYC: Pycnogenol and chronic tinnitus

Acronym
TinniPYC

Study objectives
The study aims to investigate whether daily supplementation with Pycnogenol® in capsules (150mg/day) is able to reduce the symptoms of tinnitus, improve quality of life and to affect parameters of oxidative stress in patients with chronic tinnitus for 3 months.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/12/2022, Ethics Board of St. Cyril and Methodius Hospital, University Hospital in Bratislava, Slovakia (Antolská 11, 851 07 Bratislava, SLovakia; +421 2 68672 730; eticka.komisia@pe.unb.sk), ref: EK/2/12/2022

Study design
inerventional double-blinded randomized and placebo-controlled study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Community, Medical and other records

Study type(s)
Quality of life

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
Chronic tinnitus

Interventions
Participants randomised to active or placebo group will be required to take three capsules a day for 3 months:
1. Active intervention: 50 mg of standardised extract from pine bark – Pycnogenol® per capsules

2. Placebo intervention: maltodextrin without the active substances, identically packaged as active.
Both interventions will be prepared by Horphag Research Ltd. (Geneva, Switzerland).

Eligible subjects were allocated in a 1:1 ratio to the two arms of the study (active and placebo) according to a computer-generated random sequence using block randomisation with a block-size of four. The randomisation was performed by a study statistician, who had no participant contact. Participants were enrolled and assigned sequentially to interventions by the doctor. The allocation sequence sealed in an envelope will be kept by the project coordinator in case of an emergency requirement to break the code. The allocation sequence was not available to any member of the research team until the databases had been completed and locked.

Intervention Type
Supplement

Primary outcome measure
Changes in clinical symptoms are measured by audiometry at baseline and 3 months:
1. Tinnitus intensity
2. Tinnitus noise and frequency
3. Masking tone

Secondary outcome measures
1. Quality of life measured usig Tinnitus Functional Index (TFI) questionnaires at baseline and 3 months,
2. Basic biochemical parameters (glucose, insulin, uric acid, urea), lipid profile (total cholesterol, HDL, LDL, TAG) , liver enzymes (ALT, AST, ALP), blood count and cortisol levels measured in the accredited Clinical biochemistry and haematology laboratory at baseline and 3 months after intervention,
3. Markers of oxidative stress (DNA damage, AOPP, LPx, TBARS, nitrothyrosine, total oxidant status), levels of paraoxonase with lactonase activity (PON-L) and cytokine IL-10 measured in plasma/serum or whole blood at baseline and 3 month after intervention,
4. Total antioxidant status (FRAP, TEAC) and activities of antioxidant enzymes (SOD, GPx, CAT) measured in plasma or erythrocytes lysate at baseline and 3 months of intervention.

Overall study start date
01/05/2022

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Adults aged between 18 and 70 years
2. Chronic tinnitus for a minimum of 6 months
3. Patients who are willing to sign an informed consent
4. Patients who are willing to provide two blood samples

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
80 participants, 40 in active group and 40 in placebo

Key exclusion criteria
1. Age <18 and >70 years.
2. Pregnant or breastfeeding women.
3. Patients with a history of ear surgery.
4. Patients with vestibular schwannoma hearing impairment beyond age-related sensor neurological disorder, more serious neurological or internal disease (tumour, stroke, vascular stenosis, Meniere's disorder, etc.).
5. Patients who are taking blood thinners.
6. Patients who are unable/unwilling to sign an informed consent.
7. Patients who are unable/unwilling to provide samples of biological material as needed.

Date of first enrolment
22/08/2023

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
Slovakia

Study participating centre
Faculty of Medicine and University Hospital, Comenius University Bratislava
Department of Otorhinolaryngology - Head and Neck Surgery
Antolská 11
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Study participating centre

Comenius University
Institute of Medical Chemistry, Biochemistry and Clinical Biochemistry
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Sponsor information

Organisation
Horphag Research (Switzerland)

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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
01/06/2026

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@fmed.uniba.sk

IPD sharing plan summary
Available on request