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Prospective study to assess the effect of a probiotic on microbiota composition and inflammation in women with endometriosis

Submission date
17/06/2025

Recruitment status
No longer recruiting

Registration date
18/06/2025

Overall study status
Completed

Last Edited
18/06/2025

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Endometriosis is a chronic, estrogen-dependent inflammatory disorder affecting up to 10% of reproductive-age women, associated with pelvic pain, infertility, and diminished quality of life. Emerging evidence implicates the vaginal microbiome and estrogen metabolism in the pathogenesis of endometriosis. Ligilactobacillus salivarius CECT 30632, a probiotic strain with known in vitro estrogen-modulating properties, represents a potential therapeutic strategy. This study aims to evaluate whether L. salivarius CECT 30632 complements conventional therapy by modulating systemic estrogen levels and enhancing quality of life in endometriosis management.

Who can participate?
Women aged between 18 and 45 years with endometriosis

What does the study involve?
A study will be conducted in which people are randomly given either a L. salivarius CECT 30632 supplement or a placebo (dummy) supplement, and neither they nor the researchers know who will receive which, to fairly test if the treatment works, assessing its effects, alongside standard dienogest treatment. Outcomes included vaginal microbiota composition, serum 17β-estradiol levels, immunological markers, and quality of life assessed using a questionnaire.

What are the possible benefits and risks of participating?
Women receiving the L. salivarius strain are expected to have a significant reduction in pain perception, emotional distress, and feelings of helplessness. Endometriosis-associated pain arises from a complex interplay of peripheral and central mechanisms, involving inflammation, neurogenic alterations, and hormonal dysregulation. Inflammatory mediators secreted by ectopic lesions activate nociceptive neurons in the peritoneal environment, leading to central sensitization and amplified pain perception. Chronic pain further contributes to hypothalamic-pituitary-adrenal axis dysregulation, increasing vulnerability to anxiety, depression, and pain catastrophizing. Estrogens modulate pain signalling by upregulating neurotrophic factors and inflammatory cytokines.

The possible risk is the appearance of adverse events.
To manage this, the safety of the administered product will be continuously evaluated throughout the study. To this end, at each visit, the vital signs of the patients will be measured (temperature, blood pressure, heart rate), and a physical examination will be performed. An active collection and evaluation of adverse events by the PI will also be performed.
Safety and tolerability variables:
Incidence of adverse events (AEs).
Incidence of Serious Adverse Events (SAEs)

Where is the study run from?
Exeltis Healthcare, Germany

When is the study starting and how long is it expected to run for?
May 2023 to April 2025

Who is funding the study?
Insud Pharma, Spain

Who is the main contact?
Pedro-Antonio Regidor, pedro-antonio.regidor@exeltis.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Ligilactobacillus salivarius CECT 30632 as novel adjunct therapy for endometriosis: Impact on vaginal microbiota, inflammation, 17β-estradiol and quality of life

Acronym
ENDO-1

Study objectives
The role of the vaginal microbiome in endometriosis is still poorly understood. Although the composition of the vaginal microbiota in healthy women of reproductive age may vary depending on several factors, including geographical location and ethnicity, it is generally considered to be characterized by low alpha diversity and a dominance of lactobacilli. However, conflicting results have arisen from studies evaluating potential relationships between endometriosis and the vaginal Lactobacillus population. While some have found a reduction in Lactobacillus abundance and an increased prevalence of genera such as Gardnerella and Atopobium, others have reported a Lactobacillus-dominated microbiome in affected women. Vaginal dysbiosis may drive inflammation and immune dysfunction, as microbiota alterations can activate systemic inflammation pathways, including TLR4 and NF-κB signalling.

Given that estrogen levels and inflammation are key factors in endometriosis, therapies based on live therapeutic agents targeting both aspects may represent a promising strategy for improving the management of this condition. Ligilactobacillus salivarius CECT 30632 is a strain that has demonstrated potential in improving fertility outcomes in women with habitual abortion or infertility of unknown origin. Furthermore, recent studies indicate that this strain can degrade and conjugate 17β-estradiol in vitro, making it a promising candidate, alone or in combination with hormonal therapies, for improving symptoms associated with estrogen-related gynecological conditions such as endometriosis.

Objectives:
1st: To evaluate the effect of a probiotic on the composition of the vaginal microbiota and inflammation in women with endometriosis.
2nd: To analyze the evolution of pain and estrogen levels.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/05/2023, Research Ethics Committee for Medicines of the Hospital Universitario La Paz (P.º de la Castellana, 261, Madrid, 28046, Spain; +3491 727 75 76; direccion@idipaz.es), ref: Code HULP: 6460

Study design
Pilot randomized double-blind parallel-design placebo-controlled study

Primary study design

Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital, Laboratory, University/medical school/dental school

Study type(s)
Quality of life, Treatment, Safety, Efficacy

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Evaluation of endometriosis-associated pain

Interventions
In this randomized, double-blind, placebo-controlled clinical trial, 40 women who were taking a daily oral dose of dienogest (2 mg) were randomly assigned using aleatoric randomisation with a SAS (Statistical Analysis System) software to two groups: group 1 (n = 20), to ingest a daily capsule containing ~ 9 log10 colony-forming units (CFU) of L. salivarius CECT 30632; and, group 2 (n = 20), to ingest a placebo capsule devoid of the bacterial strain. The trial lasted for 16 weeks, with hospital visits at baseline (V1) and at the end of the study (V2).

Intervention Type
Supplement

Primary outcome measure
The following primary outcome measures are assessed at baseline (V1) and the end of the study (V2):
1. Vaginal microbiota measured by DNA extraction from vaginal samples and sequence analysis using the Illumina MiSeq pair-end protocol
2. Inflammation, captured via the immunological analysis of serum levels of interleukin (IL)-8, IL-10, tumoral necrosis factor (TNF)-α, vascular endothelial growth factor A (VEGF-A), and transforming growth factor β2 (TGF-β2) using a Luminex XMAP™ Technology analyser

Secondary outcome measures
The following secondary outcome measures are assessed at baseline (V1) and the end of the study (V2):
1. Quality of life measured using the Endometriosis Health Profile-30 (EHP-30) questionnaire
2. Serum 17β-estradiol levels were measured using an immunoassay by chemiluminometric technology performed in an Atellica® IM analyzer

Overall study start date
11/05/2023

Completion date
30/04/2025

Eligibility

Key inclusion criteria
1. Women between 18 and 45 years of age
2. Endometriosis diagnosed by clinical criteria: visual tests, ultrasound, symptomatology (including pelvic pain, with a score ≥ 3 on the NRS scale)
3. Women of childbearing age must have a negative pregnancy test prior to inclusion in the study and must commit to oral contraceptive treatment containing a progestin (dienogest 2 mg) for the entire duration of the study and continue until the end of indicated treatment
4. Signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants
40

Total final enrolment
40

Key exclusion criteria
1. Current BMI> 30 kg/m2
2. Any known endometrial pathology other than endometriosis.
3. Polycystic ovary syndrome
4. Ovulatory dysfunction
5. Immunosuppression
6. Patients with severe acute or chronic disease (e.g., pancreatitis, hypertriglyceridemia, liver disease, benign or malignant liver tumor, sex hormone-dependent genital or breast malignancies)
7. History of serious cardiovascular events
8. Uncontrolled hypertension or diabetes
9. Hypersensitivity, allergy or known intolerance to any of the components of the products under investigation.
10. Consumption of medications, complements or food supplements that could have an impact on the development of the study, such as antibiotics, other pro- and prebiotics, laxatives, etc. during the course of the study
11. Undiagnosed abnormal vaginal bleeding
12. Clinical evidence of neuropathy

13. History of pelvic inflammatory diseases
14. Patients with autoimmune diseases (including Crohn's disease)
15. Pregnancy and/or breastfeeding for the duration of the study
16. Postmenopausal patients
17. Participation in any other clinical trial 30 days prior to the start of the study
18. Women who, at the investigator's discretion, do not present the conditions to be able to participate in the study safely

Date of first enrolment
01/08/2023

Date of final enrolment
01/12/2024

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Quironsalud de Málaga, Servicio de Ginecología y Obstetricia
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Study participating centre
Hospital Universitario La Paz, Servicio de Ginecología y Obstetricia
Paseo de la Castellana 261
Madrid
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Sponsor information

Organisation
Exeltis Healthcare

Sponsor details
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Insud Pharma

Results and Publications

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

Intention to publish date
20/06/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request by MD PhD Pedro-Antonio Regidor, pedro-antonio.regidor@exeltis.com

• The type of data that will be shared: Results of the trial
• Timing for availability: Publication
• Whether consent from participants was required and obtained: Yes
• Comments on data anonymization: They will be totally anonymous
• Any ethical or legal restrictions: No
• Any additional comments: No

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results			18/06/2025	No	No
Participant information sheet	version 1.0	10/04/2023	18/06/2025	No	Yes