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Vaginal colonization by orally consumed lactobacilli in healthy women

Submission date
08/09/2020

Recruitment status
No longer recruiting

Registration date
16/09/2020

Overall study status
Completed

Last Edited
21/02/2023

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
This study has been designed to investigate the effect of a probiotic supplement on the natural bacteria of the vagina in healthy women. A healthy environment (microflora) in the vagina is supported by the presence of large numbers of certain bacteria called lactobacilli. Lower numbers of these bacteria have been associated with a risk of health problems such as bacterial vaginosis (BV), yeast infections such as thrush, and urinary tract infections (UTIs).
It is believed that taking a regular probiotic supplement containing lactobacilli by mouth can help increase the numbers of lactobacillus bacteria in the vagina. The reason for this is not entirely clear, but initial studies in both mice and healthy women have successfully shown this effect on the vaginal microflora. While similar studies have already been done, this study is different because it will look at the effects of only two specific lactobacillus bacteria in the probiotic supplement.

Who can participate?
Caucasian women between the age of 18 and 50 who have not have had any vaginal infections in the past 6 months and are willing to use a valid form of contraception throughout the study.

What does the study involve?
The study involves a total of five clinic visits over a period of up to about 2 months. Participants are randomly allocated to one of two groups. One group will be given capsules containing lactobacillus bacteria and the second group will be given placebo (dummy) capsules. During the supplementation period (14 days between Visit 2 and Visit 4) each participant will consume one capsule orally every day after breakfast. The numbers of lactobacillus bacteria in the vagina is measured at the start of the study and at day 7, day 14 and day 21.

What are the possible benefits and risks of participating?
There are no definite benefits for taking part in this study. It is possible that the probiotic supplement could have an effect on helping maintain a vaginal microflora considered healthy. There are no specific risks are anticipated in relation to the study product when taken by otherwise healthy people. Any potential side effects are unexpected but may include mild and

transient symptoms related to the digestive tract, such as tummy discomfort, bloating, or wind. As with any food product, there is a possible risk of allergy to the ingredients of the study product.

Where is the study run from?
CPS Research (UK)

When is the study starting and how long is it expected to run for?
May 2020 to March 2021

Who is funding the study?
Danisco Sweeteners Oy (Finland)

Who is the main contact?
Anna Lyra, anna.h.lyra@iff.com

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
287782

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
NH-05173, IRAS 287782

Study information

Scientific Title

Vaginal colonization of lactobacillus acidophilus and lacticaseibacillus rhamnosus in healthy females: a double-blind, randomized, placebo-controlled trial

Acronym
SG-FREYA

Study objectives
The primary objective of the study is to show the difference between verum supplementation and placebo in the vaginal colonization of L. acidophilus and L. rhamnosus during and after 2 weeks supplementation of verum containing L. acidophilus and L. rhamnosus.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/10/2020, East of Scotland Research Ethics Service REC 1 (Ninewells Hospital & Medical School, Tayside Medical Science Centre (TASC), Residency Block, Level 3, George Pirie Way, Dundee, DD1 9SY, UK; +44 (0)1382 383871; Tay.eosres@nhs.net), REC ref: 20/ES/0089

Study design
Two-arm double-blind randomized placebo-controlled parallel-group single-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Vaginal health

Interventions
Participants will be screened at the screening visit (Visit 1) to check that all the inclusion criteria and none of the exclusion criteria are met. The eligibility will be confirmed before Visit 2 based on the laboratory results (vaginal swab: Nugent score (for BV) and Chlamydia and trichomoniasis) taken at Visit 1.

Randomization will be carried out with a computer-generated random allocation of study participants to one of two treatment groups in equal proportions using randomly permuted blocks.

After randomization at baseline (Visit 2), two groups will be provided with IP (dietary supplement): one group will be supplemented with capsules containing a mixture of the active ingredients at the intended daily dose of 1 x 10(10) CFUs probiotics L. acidophilus and L. rhamnosus mixed with a carrier (maltodextrin) and a second group will consume placebo capsules containing carrier only. At randomization (Visit 2) and at Visit 3, each participant will receive one bottle of 10 capsules including capsules for each 7-day supplementation period.

During the supplementation period (14 days between Visit 2 and Visit 4) each participant will consume 1 capsule orally every day after breakfast, starting from the day after (Day 1) the baseline visit (Visit 2).

Intervention Type
Supplement

Primary outcome measure
Vaginal colonization of L. acidophilus and L. rhamnosus measured with quantitative PCR at baseline, day 7, day 14 and day 21

Secondary outcome measures
Vaginal pH measured with pH test strips baseline, day 7, day 14 and day 21

Exploratory analyses include assessment of vaginal microbiota composition and immunological markers

Overall study start date
07/05/2020

Completion date
24/03/2021

Eligibility

Key inclusion criteria
1. Female
2. Age 18–50 years (fertile age)
3. Caucasian
4. No vaginal infections within the previous 6 months
5. Has not participated in another investigational drug clinical trial within 1 month (30 days) or received an investigational drug within the last month (30 days) before the start of screening
6. No significant changes in daily routines related to dietary/activity patterns
7. Willingness to take dietary supplements
8. Valid contraception for the duration of the study:
8.1. Use of oral, (estrogen and progesterone), injected or implanted hormonal methods of contraception or placement of an intrauterine device (IUD) or intrauterine system (IUS), or other forms of hormonal contraception that have comparable efficacy
8.2. Total abstinence (when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception
8.3. Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy), total hysterectomy, or bilateral tubal ligation at least six weeks before taking study treatment.

8.4. Male sterilization (at least 6 months prior to screening). For female subjects on the study, the vasectomized male partner should be the sole partner for that subject
8.5. Barrier contraceptive (condoms)
9. Willingness to collaboration in completing the binding parts of the study protocol

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
50

Total final enrolment
50

Key exclusion criteria
1. Vaginal or urinary complaints within 3 months
2. Vaginal pH > 4.5
3. Pregnant or planning pregnancy
4. Breastfeeding
5. History of significant vulvo-vaginal pathological conditions
6. Antibiotic usage during last 3 months
7. Oral corticosteroid usage during last 3 months
8. Use of vulvo-vaginal medication
9. Acquired or congenital immune deficiency
10. Recent history of radiotherapy (within 2 years)
11. Current or prolonged (more than 1 month in last 2 years) use of corticosteroids or other immune modulating medication. Inhaled corticosteroids for asthma are not considered as an exclusion if their usage has begun more than 3 months prior to recruitment
12. Habitual use of probiotic supplementation
13. Menstrual irregularities including menopause
14. On-going diagnosed disease which in the opinion of the investigator makes the participant unfit for the study
15. Intolerance to any of the study products
16. History of alcohol abuse within 2 years
17. History of drug abuse within 2 years
18. Unable to communicate with the investigator
19. Positive culture from swabs at visit 1 or Nugent score >3 (added 05/01/2021)

Date of first enrolment
05/11/2020

Date of final enrolment

28/02/2021

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
CPS Research
3 Todd Campus
West of Scotland Science Park
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Sponsor information

Organisation
Danisco Sweeteners Oy (Finland)

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Sponsor type
Industry

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ROR
https://ror.org/02nqcmv36

Funder(s)

Funder type
Industry

Funder Name
Danisco Sweeteners Oy (Finland)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. Full study protocol and statistical analyses plan won't be available, but all the study methods and statistical analyses will be reported in the publication in detail.

Intention to publish date
31/05/2023

Individual participant data (IPD) sharing plan
The Trial Master File of the study, containing pseudo-anonymized data, will be stored by the Sponsor for 25 years. At the moment, it is not planned to make the pseudo-anonymized data publicly available.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/02/2023	21/02/2023	Yes	No
HRA research summary			28/06/2023	No	No