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Evaluation of the impact of fermented milk containing Lactobacillus casei strain Shirota (LcS) on stool consistency

Submission date
06/06/2019

Recruitment status
No longer recruiting

Registration date
14/06/2019

Overall study status
Completed

Last Edited
01/08/2024

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
In the guidance for evaluating health claims on foods related to gut and immune function published by the European Food Safety Authority (EFSA), it is stated that softer stool is a beneficial effect for our health, provided it does not result in diarrhoea. In previous studies, it was observed that continuous consumption of the fermented milk containing Lactobacillus casei strain Shirota (Yakult®) contributed to reducing the incidence of hard stools by softening stools. In addition, when focused on the participants who frequently produced hard stools, the frequency of softer stools (not diarrhoea) was significantly increased in the Yakult® group than in the placebo group. The results can be evidence to show the efficacy of Yakult®, but there remains several issues to be solved. In the previous studies, the Bristol Stool Form Scale (BSFS) was used to evaluate the change of stool hardness. This scale was originally validated as a surrogate measure for gastrointestinal transit time, and was also admitted as a validated questionnaire to evaluate stool hardness. However, the evaluation by the BSFS is subjective and affected by a participant's feeling in defecation because the questionnaire is filled out by the participant him/herself. Recently a new method to directly measure stool hardness was validated using a texture analyser (TA.XT Express Texture Analyser; Stable Micro Systems Ltd.). This new method can be used to obtain objective and reproducible data of changes in stool hardness over time. The aim of this study is to evaluate the impact of Yakult® on stool hardness using the texture analyser and find out whether Yakult® consumption has a beneficial effect.

Who can participate?
Healthy volunteers aged 18-65 who frequently produce hard stools

What does the study involve?
The BSFS data is collected from all participants for 2 weeks. Then, participants who frequently produce hard stools (BSFS 1 and 2 stools with the frequency of 50% or more) are randomly allocated to the probiotic group or the placebo group so that the proportion of gender, age and potentially BMI are equal within both groups. Participants in the probiotic group are asked to consume one bottle of fermented milk containing LcS daily for 8 weeks. Participants in the placebo group are asked to consume one bottle of placebo (non-fermented milk without LcS)

daily for 8 weeks. All participants are asked to collect stool samples at three timepoints (before probiotic/placebo consumption, and 4 and 8 weeks after starting probiotic/placebo consumption) for three consecutive days (72 hours), and to record BSFS data for all defecations using an online questionnaire until the end of the study.

What are the possible benefits and risks of participating?
Participants in the probiotic group might produce softer stools. There are no risks of taking part in this study. Yakult® has a history of safe use in the European population for more than 20 years. Therefore, it's safe for the participants to consume Yakult® or the placebo.

Where is the study run from?
SGS Life Sciences Clinical Pharmacology Unit Antwerpen (Belgium) and AZ Sint-Maarten (Belgium)

When is the study starting and how long is it expected to run for?
October 2018 to March 2020

Who is funding the study?
Yakult Honsha European Research Centre for Microbiology ESV (Japan)

Who is the main contact?
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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
YHER19-SGS

Study information

Scientific Title
Evaluation of the impact of fermented milk containing Lactobacillus casei strain Shirota (LcS) on stool consistency

Study objectives
Daily consumption of a fermented milk containing LcS produces softer stools than daily consumption of a placebo (non-fermented milk without LcS).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/05/2019, Commissie voor Medische Ethiek ZNA (ZNA Koningin Paola Kinderziekenhuis, Lindendreef 1, 2020 Antwerpen, Belgium; Tel: +32 (0)3/280 34 29 or +32 (0)3 /280 34 28; Email: ethische.commissie@zna.be)

Study design
Randomized double-blind placebo-controlled parallel-group multi-centre study with two arms

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Stool consistency

Interventions
Sixty four healthy subjects who frequently produce hard stool (Bristol Stool Form Scale score 1 and 2 stools with the frequency of 50% or more during 2 weeks of the screening data collection period) will be randomised to the probiotic group or the placebo group in a 1:1 ratio. Subjects in

the probiotic group will receive one bottle of fermented milk containing LcS daily for 8 weeks. Subjects in the placebo group will receive one bottle of placebo (non-fermented milk without LcS) daily for 8 weeks.

Intervention Type
Other

Primary outcome measure
Stool consistency measured by the texture analyser (TA.XT Express Texture Analyser) before consumption of investigational product (IP), and 4 and 8 weeks after starting IP consumption

Secondary outcome measures
1. Bowel habit and stool consistency measured using the Bristol Stool Form Scale score for all defecations using online questionnaire from after allocation until the end of the study

Measured from stool samples collected before consumption of investigational product (IP), and 4 and 8 weeks after starting IP consumption:
2. Stool amount measured by weighing
3. Stool water content measured by subtracting dried stool weight from raw stool weight
4. Stool pH measured directly using pH meter InLab®Solids
5. Stool mucin, stool lipids and stool bile acids measured by commercial ELISA kits
6. Stool microbiota analyzed by 16S rRNA sequencing method
7. Stool organic acids and stool putrefactive substances measured by High Performance Liquid Chromatograph (HPLC)

Overall study start date
01/10/2018

Completion date
31/03/2020

Eligibility

Key inclusion criteria
1. Informed consent obtained before any study-related activities
2. Healthy female or male aged 18–65 years (inclusive)
3. Produces hard stool (BS1 and 2 stools), with a frequency of 50% or more during 2 weeks of screening data period
4. Does not take probiotics 2 weeks before the start of screening data collection. If the patient takes probiotics, a washout period of 2 weeks is needed
5. Is willing and able to collect every stool at home during 3 consecutive days and this 3 times during the treatment period, to store the samples in appropriate conditions and to return the samples within the required timeframe
6. Is willing and able to complete a diary during the screening, baseline and treatment period in order to collect information about the form of the stools (based on the Bristol Stool Form Scale classification) and bowel habit
7. Prepared not to change the current drinking, eating, smoking and exercising habits during the course of the study
8. Understands the Dutch or English language (reading, writing, speaking)

Participant type(s)

Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
64 participants (probiotic group: 32 participants, placebo group: 32 participants)

Total final enrolment
64

Key exclusion criteria
1. Language barrier, mental or legal incapacity, unwillingness or inability to understand or not being able to participate in the study
2. Is vegetarian or vegan
3. Is treated (i.e., currently treated, treated within 1 month before screening) by a doctor for her /his constipation
4. Has any history of gastrointestinal surgery except for appendectomy
5. Has any history of chronic/severe gastrointestinal disorders
6. Females of childbearing potential who are pregnant, breastfeeding or intend to become pregnant or are not using adequate contraceptive methods (e.g., oral contraceptive, condom, intrauterine device, abstinence)
7. Is unable to refrain from or anticipates the use of antibiotics and/or laxatives
8. Has any history of drug and/or alcohol abuse
9. Has milk allergies
10. Is intolerant to lactose
11. Any clinically significant disease which in the Investigator’s opinion could interfere with the safety of study participants or with the results of the study
12. Use of disallowed concomitant medications and concomitant products within 2 weeks before the screening period, depending if a wash out period for probiotics is needed
13. Cancer (past or present, except basal cell skin cancer or squamous cell skin cancer), which in the Investigator’s opinion could interfere with the results of the study
14. Previous participation in this study. Participation is defined as screened. Re-screening is therefore not allowed
15. Participation in another interventional clinical study or receipt of any investigational product within 1 month before the screening period

Date of first enrolment
12/06/2019

Date of final enrolment
23/08/2019

Locations

Countries of recruitment
Belgium

Study participating centre
SGS Life Sciences Clinical Pharmacology Unit Antwerpen
Lange Beeldekensstraat 267
Antwerpen
Belgium
2060

Study participating centre
AZ Sint-Maarten
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Sponsor information

Organisation
Yakult Honsha European Research Centre for Microbiology ESV

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Sponsor type
Industry

Website
http://www.yakult.co.jp

ROR
https://ror.org/03wmnrc91

Funder(s)

Funder type

Industry

Funder Name
Yakult Honsha

Alternative Name(s)
Yakult

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Japan

Results and Publications

Publication and dissemination plan
Publication is planned in a peer-reviewed journal.

Intention to publish date
30/11/2022

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		30/07/2024	01/08/2024	Yes	No