Modulation of small intestinal microbial composition and activity, systemic immune adaptation and blood transcriptional changes induced by 2-wks consumption with 2 fermented milk products; a randomized, exploratory, cross-over, double blind, controlled study in ileostomy patients

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Rationale: to determine the small intestinal microbiota response in humans to dietary interventions for two consecutive weeks, and to relate this to parameters of intestinal barrier function and immune and metabolic responses in blood, as functional...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON45768

Source
ToetsingOnline

Brief title
Modulation of microbial composition in ileostomy patients

Condition

- Gastrointestinal conditions NEC

Synonym
colectomy, ileostomy

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Danone Nutricia Research, Plaiseau Cedex, Frankrijk,Danone Nutricia Research;Palaiseau Cedex;Frankrijk

Intervention

Keyword: ileostomy, microbiota, small intestine

Outcome measures

Primary outcome

* To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on temporal microbial composition and activity in the small intestine.

Secondary outcome

To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on small intestinal permeability;

* To assess the gene transcription response in blood to consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks;

* To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on the levels of a panel of peripheral blood biomarkers related to immune, metabolic and hormonal status;
* To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on the level of whole blood immune responsiveness to a panel of standardized stimuli ex vivo;
* To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on morning urine metabolome profiles;
* To assess the effects of consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on peripheral blood metabolome profiles;
* To assess the relative survival of bacterial strains from milk fermented by Lactobacillus rhamnosus CNCM I-3690 and from milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 after transit through the gastrointestinal tract up to the ileostomy;
* To assess the effects of consumption of milk fermented by Lactobacillus

rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks on short chain fatty acid profiles in ileal effluent.

* To assess gastrointestinal symptoms and occurrence and severity of adverse events during and after consumption of milk fermented by Lactobacillus rhamnosus CNCM I-3690 and of milk fermented by a yogurt symbiosis of Streptococcus thermophilus CNCM I-1630 and Lactobacillus bulgaricus CNCM I-1519 for 2 weeks.

Study description

Background summary

Although yogurts have been an important part of human diet for thousands years and are part of the official nutritional recommendation in many countries, the mechanism of beneficial action exerted by yogurt cultures is still poorly known. It is particularly interesting to know whether specific yogurt starter strains resist to digestive stress conditions and survive the passage through the stomach and the small intestine, where their potential beneficial effect is mostly probable to take place. Today, the research on survival rate of yogurt strains in human digestive tract indicates that this trait might be strain dependent.
The mucosal responses to intake of probiotics are more pronounced in the small intestine as compared to the large intestine, which is in agreement with the conserved and biologically coherent transcriptional responses detected in human duodenal mucosa upon consumption of probiotic products. Analogously, the small intestine is of much greater importance compared to the large intestine for the absorption of nutrients from the diet, and metabolic effects have recently been suggested to be orchestrated most dominantly by the small intestine.
Therefore, to obtain more insight in the role of the small intestine microbiota and its modulation by fermented dairy products in steering local and systemic metabolic and immune related functions is of importance to better understand the role of such (health-promoting) food products.

Study objective

Rationale: to determine the small intestinal microbiota response in humans to

dietary interventions for two consecutive weeks, and to relate this to parameters of intestinal barrier function and immune and metabolic responses in blood, as functional outcome parameters of host physiology.

Study design

randomized, cross-over, double blind, controlled study

Intervention

Fermented milk products

Study burden and risks

Intake of study products once daily during three intervention periods of two weeks each. The study products are fermented milk products which are safe for human consumption. Collection of urine and ileal excretions. Blood sampling. Filling in questionnaires.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Ileostomy installed at least 2 years prior to participation
- Free of any complications originating from the colectomy procedure for at least 1 yr prior to participation, with the exception of possible skin irritation at the location of the stoma
- BMI from 18 till 28 kg/m2
- Age from 18 till 70 years
- Available for entire study protocol:
- Test days at university facility
- Being able to collect ileal effluent samples at regular basis over the required period of time
- Compliant to dietary restrictions and reliable for sample collection
- Subject who regularly consumes dairy fermented products containing live bacteria
- For female: If of child bearing potential, female subjects must be using or complying with methods of contraception (such as oral birth control pills, intra-uterine device, double barrier methods (like condoms and spermicide, etc.)
- Subject, upon briefing of the content of the present study, fully understanding and agreeing to its objective and having given written (dated and signed) informed consent form to take part in the study

Exclusion criteria

- History of cardiovascular, respiratory, urogenital, hepatic, haematological / immunologic, HEENT (head, ears, eyes, nose, throat), dermatological/connective tissue, musculoskeletal, metabolic/nutritional, endocrine, neurological diseases, allergy, laboratory assessments which might limit participation in or completion of the study protocol, and/or major surgery with the exception of total colectomy, hysterectomy and/or appendectomy.
- Abnormal/artificial heart valves, history of rheumatic heart disease or of infectious endocarditis, cardiac malformation
- Subject with known lactose intolerance or with known or suspected allergy or hypersensitivity to any component of the study product(s) (milk protein for example) + sucrose + rhamnose
- Subject who had any surgery or intervention requiring a general anaesthesia in the preceding 4 weeks, or who plans to have one during the course of the study
- Subject that have had dental surgery in the last 4 weeks or plan to have dental surgery during the course of the study, excluding care of tooth decay
- Severe gastrointestinal symptoms. In case of mild gastrointestinal symptoms, the principal investigator and the medically responsible MD will judge eligibility to participate.
- Removal of more than 15 cm of the ileum during or at any moment after the colectomy

procedure
- Abdominal surgery interfering with gastrointestinal function, upon judgment of the principal investigator and the medically responsible MD
- Self-admitted HIV-positive status
- Use of medication, including proton pump inhibitors, non-steroidal anti-inflammatory drugs interfering with endpoints (to be determined by the principal investigator and the medically responsible MD; but except oral contraceptives), within 14 days prior to and during participation.
- Use of antioxidants, minerals and vitamin supplements available in pharmacies, drugstores, food markets or in alternative medicine interfering with endpoints (to be determined by the principal investigator and the medically responsible MD), within 14 days prior to and during participation.
- Consumption of any probiotic or prebiotic supplements or pre- and probiotics containing food products, investigational drugs or participation in any scientific intervention study which may interfere with this study (to be decided by the principal investigator), in the 4 weeks prior to the study and during study participation (E4 PreProbiotics).
- Use of antibiotics in the 4 weeks prior to the start of study and during study participation
- Known pregnancy (assessed by a pregnancy test before start of study), lactation
- Abuse of products: alcohol (> 20 alcohol units per week) and drugs
- Blood donation within 3 months before study period
- History of any side effects towards intake of pro- or prebiotic supplements of any kind.
- Prohibited use of pro-, pre- or synbiotics during study period and three months prior to start of study. A list with forbidden products will be provided.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-10-2016

Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	20-07-2016
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	21-04-2017
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL58002.072.16

Study results

Date completed:	27-10-2017
Actual enrolment:	16