A randomized, double-blind, placebo-controlled crossover study to assess the effect of 12-week fibre supplementation on mixed-meal challenge response in adults

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Primary ObjectiveTo relate microbiome modulation by dietary fibre supplementation, as measured by 16S rRNA sequencing, to changes in response to a mixed-meal metabolic challenge (PhenFlex) as measured by composite biomarker score.Secondary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55244

Source
ToetsingOnline

Brief title
Effect of fibre supplementation on mixed-meal challenge response.

Condition

- Other condition
- Immune disorders NEC
- Metabolism disorders NEC

Synonym
Health status

Health condition

Health status

Research involving
Human

Sponsors and support

Primary sponsor: Centre for Human Drug Research
Source(s) of monetary or material Support: A consortium consisting of CHDR;TNO;DSM and TKI Agrifoods

Intervention

Keyword: Fibre, Microvascular

Outcome measures

Primary outcome

Primary endpoints

* Microbiome changes measured using 16S rRNA sequencing at baseline and at time points as defined in table 1 and 2.

* Response to challenge of metabolic and inflammatory biomarkers including but not limited to non-esterified fatty acids (NEFAs), glucose, insulin, triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol, interleukin-6, -8 and -10, tumour necrosis factor alpha (TNF-*), high-sensitivity C-reactive protein (hs-CRP), serum amyloid A (SAA), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyltransferase (GGT).

Secondary outcome

Secondary endpoints

* Baseline and post-intervention metabolic and inflammatory biomarkers including but not limited to NEFAs, glucose, insulin, TG, HDL, LDL, total

cholesterol, interleukin-6, -8 and -10, TNF-*, hs-CRP, SAA, ALT, AST and GGT.

* In vitro culturing of stool through the TNO I-screen platform and faecal SCFA

content at baseline and before the second treatment period.

Study description

Background summary

Improving healthy physiological processes through nutritional intervention, as opposed to restoring physiology after disease occurrence, is an important new avenue for the reduction of disease burden in the population. A relatively new target for interventions is the gut microbiome. Although the role of the human microbiome in health and disease is widely acknowledged, specific physiological mechanisms through which it can affect human health and disease have yet to be fully elucidated.

Study objective

Primary Objective
To relate microbiome modulation by dietary fibre supplementation, as measured by 16S rRNA sequencing, to changes in response to a mixed-meal metabolic challenge (PhenFlex) as measured by composite biomarker score.
Secondary Objectives
To investigate whether results of in vitro microbiome culturing on the I-screen platform are comparable to in vivo 16S rRNA sequencing and are affected by fibre supplementation.
To investigate whether fibre supplementation affects basal metabolic and inflammatory biomarkers and their response to mixed-meal metabolic challenge.

Exploratory Objectives
To investigate the effect of dietary fibre on mood, general health and health perception.
To investigate whether fibre supplementation affects basal endothelial function and response of endothelial function to mixed-meal metabolic challenge.
To investigate the relation between oral microbiome and gut microbiome, and the effects of mixed meal challenge on the oral microbiome.
To investigate the relationship between B cell subsets and gut microbiome function and modulation.
To investigate the effect of mixed-meal metabolic challenge on biomarkers of cellular stress.
To investigate the effect of mixed-meal metabolic challenge on

electrocardiographic indices.

Study design

A randomized, double blind, placebo-controlled crossover study with 12-week treatment periods separated by 8 weeks of washout. Mixed meal challenge tests will be conducted before and at the end of both treatment periods. The first 20 subjects included (1:1 randomized over treatment arms) will have additional endothelial testing at baseline and during PhenFlex challenges. Baseline microbiome analysis will be conducted before both treatment periods, and during treatment and washout periods subjects will send faecal samples taken at home to CHDR. 4 follow-up phone calls at week 4, 8, 24 and 28 will be conducted for questionnaires and adverse event monitoring. End of study will be after the final mixed-meal challenge at the end of the second treatment period.

Intervention

Investigational fibre mixture (active treatment)
The study product is a fibre mixture consisting of a mix of 10 g of Acacia Gum (AG) and 3 g of carrot fibre (KaroPRO) taken p.o. o.d. in powder form for a total of approximately 10 g of dietary fibre per day.

Comparative drug (placebo)
Powder consisting of 13 g of digestible carbohydrates with taste and colour indistinguishable from investigational fibre mixture.

Study burden and risks

The risk associated with the administration of a combination of AG and KaroPRO in humans are considered to be negligible, since no toxic effects of dietary fibre intake have been observed and the components of both ingredients are part of the normal human diet in similar or higher doses. Side-effects of high dietary fibre intake are increased intestinal gas production inducing bloating, as well as an increase in number of bowel movements.

The fibre mixture is expected to have microbiome-changing potential and induce changes in production of bacterial metabolites. Any observed modulation of physiological processes in the test subjects is expected to be subtle, since dosage will not exceed the minimum recommended intake of dietary fibre in the general population. Among the health benefits from dietary fibre intake recognised by various food safety agencies such as the FDA and EFSA are postprandial blood glucose attenuation, postprandial blood cholesterol attenuation and improved laxation. We expect that participating volunteers will benefit from increased consumption of the fibres within the context of this study. Effects of dietary fibre supplementation are reversible, with return to

baseline occurring as early as 3 weeks after intervention in some studies.

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

1. Signed informed consent prior to any study-mandated procedure.
2. Healthy male or female subjects, between 45 and 70 years of age, inclusive.
3. Female subjects must be of non-childbearing potential (postmenopausal for at least 12 months prior to screening or documented surgically sterile).
4. BMI 25-30 kg/m2
5. Fibre intake below recommended limits as assessed by dietary fibre intake short food frequency questionnaire (DFI-FFQ).
6. Has the ability to communicate well with the Investigator in the Dutch

language and willing to comply with the study restrictions.

Exclusion criteria

1. Evidence of any active or chronic disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and 12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
2. Chronic diseases that can affect study parameters, including but not limited to metabolic syndrome, chronic obstructive pulmonary disease, diabetes mellitus, auto-immune disease, cardiovascular disease, cerebrovascular disease, gastrointestinal disease or history of abdominal surgery with removal of (part of) small or large intestine, or any known condition that can interfere with treatment compliance such as psychiatric disease or drug dependence.
3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.
4. Systolic blood pressure (SBP) greater than 180 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 120 or less than 50 mm Hg at screening.
5. Abnormal findings in the resting ECG at screening defined as:
a. QTcF> 450 for males or QTcF>470 for females or QTcF < 300 ms;
b. Personal or family history of congenital long QT syndrome or sudden death;
c. Evidence of atrial fibrillation, atrial flutter, complete branch block, Wolf-Parkinson-White Syndrome, or history of cardiac pacemaker.
6. Use of antibiotics, antacids, laxatives, statins, anti-diarrheal, immunomodulatory or antidiabetic medication <3 months before start of study.
7. Use of any medication or vitamin, mineral, herbal, and dietary supplements within 7 days of study product administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator.
8. Vegan, macrobiotic, slimming or medically prescribed diet up to 3 months prior to the first administration.
9. History of food allergies or intolerances or any confirmed significant allergic reactions (urticarial or anaphylaxis) against any drug or multiple documented drug allergies.
10. Participation in an investigational drug or device study within 3 months prior to first dosing.
11. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent, or positive test for drugs of abuse at screening or pre-dose.

12. Active smoker up to 15 years prior to the screening visit.
13. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2020
Enrollment:	64
Type:	Actual

Ethics review

Approved WMO Date:	23-01-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	11-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL71723.056.19