Effect of prebiotic fibres on Intestinal Health and Functioning

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To study effects of AXOS (1) on gut health including among other parameters intestinal transit time, fecal cytotoxicity, pH, inflammatory markers, short-chain fatty acids and microbiota composition), gut permeability and gut functioning (bloating,...

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

Summary

ID

NL-OMON42114

Source
ToetsingOnline

Brief title
Prebiotics and metabolism

Condition

- Gastrointestinal conditions NEC
- Metabolism disorders NEC

Synonym
Prevention of gastro-intestinal and chronic rmetabolic diseases

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Top Institute Food and Nutrition (TIFN)

Intervention

Keyword: arabinoxylan-oligosaccharide, intestinal health, prebiotic fibre, whole gut transit time

Outcome measures

Primary outcome

* Whole gut transit measured by clinically validated method with radio-opaque marker. A capsule containing 10 radio-opaque markers is ingested for 6 consecutive days to distribute the markers evenly throughout the body. On day seven, the radio-opaque markers are visible on fluoroscopy images and numbers of retained markers are counted. Whole gut transit is determined by dividing the number of retained markers by the daily dosage number.

Secondary outcome

Markers of gastrointestinal health:

* Fecal bulking, defecation frequency and stool consistency. This will be measured by fecal weight and a questionnaire on gastro-intestinal symptoms, including the severity and frequency of symptoms associated with intestinal functioning such as bloating, rumbling, defecation frequency and the stool consistency based on the Bristol stool chart
* Gastric emptying and oro-cecal transit time will be measured based on 13C-octanoic acid breath test and Inulin breath test, respectively. Determining gastric emptying rate and oro-cecal transit is important to identify differential effects on the upper or lower gastrointestinal transit
* in vivo* gut barrier function by means of a multi-sugar assay for site-specific gastro-intestinal permeability analysis, to identify differential

effects in upper and lower gastrointestinal permeability

* Microbiota composition (16 r RNA gene sequencing, HITChip) and fecal SCFA (LCMS) will provide insights in prebiotic-induced effect on microbiota composition and activity

* fecal water cytotoxicity (CytoTox*ONE Homogeneous Membrane Integrity Assay) fecal pH and inflammatory markers (e.g. calprotectin) are validated biomarkers that define the gastrointestinal health status

Markers of metabolic health:

* Energy expenditure and substrate oxidation before and after a standardized breakfast meal test (indirect calorimetry)

* Circulating Metabolites (glucose free fatty acids, triglycerides) and hormones (insulin, GLP-1, PYY and angiopoietin-like 4 ANGPTL4) during fasting and after the mixed high fat meal test

* Systemic Inflammatory markers like TNF-*, IL-6, IL-1, Lipopolysaccharide binding protein (LBP)

* Body weight, BMI and body compositions (bioimpedance)

* Adipose tissue gene and/or protein expression involved in functional pathways is determined to detect a potential effect of microbiota modulation on adipose function and substrate metabolism

Questionnaires:

* Questionnaires on quality of life and activity

Study description

Background summary

Dietary fibre intake provides many health benefits. A sufficient or generous intake of dietary fibre reduces the risk for developing coronary heart disease, stroke, hypertension, diabetes, obesity and certain gastro-intestinal disorders. Increased consumption of dietary fibre has been shown to improve serum lipid concentrations, reduced blood pressure, improve blood glucose control in diabetes, promotes regularity, helps in losing weight and improves immune function. The most pronounced effect of dietary fibers is on gastrointestinal transit (GI) time and fecal bulking, attributed mostly to insoluble, non-fermentable dietary fibers such as wheat bran. GI transit is an important parameter of gut health relevant for many physiological and metabolic processes. Other dietary fibers such as soluble and fermentable fibers function as prebiotics, which are fermented in the colon and thus positively affect microbiota composition and activity. However, little is known about effect of prebiotic fibers on gastrointestinal transit and the metabolic consequences. Additionally, potential shifts in the microbiome have not been evaluated at a large scale with *state-of the art* metagenomic profiling techniques. In this study, we investigate the effect of prebiotic fiber arabinoxylan-oligosaccharides (AXOS) on gastrointestinal transit time and markers of gut health and relate them to the metabolic parameters. Integrating gut physiology and microbiome with host parameters of systemic inflammation, glucose, lipid and energy metabolism would yield unique new insights that may hold great relevance in the prevention of chronic metabolic diseases. This is of particular relevance for the wheat bran derived arabinoxylans, which have been reported to have a distinct effect on short chain fatty acid (SCFA) production by the microbiota, and affect satiety and glycemic and insulinemic profiles in the human host.

Hypothesis:
We hypothesize that the daily oral intake of AXOS might modify gastrointestinal transit and microbiota composition and activity and that these factors (and their interaction) are related to an improvement of gastrointestinal and metabolic health

Study objective

To study effects of AXOS (1) on gut health including among other parameters intestinal transit time, fecal cytotoxicity, pH, inflammatory markers, short-chain fatty acids and microbiota composition), gut permeability and gut functioning (bloating, rumbling, stool frequency, stool consistency (based on the Bristol stool chart) and flatulence) (2) on systemic markers of host metabolic and immune health including substrate and energy expenditure,

circulating metabolites, inflammatory and hormone profiles, adipose tissue markers (3) to relate parameters of gut health and functioning and microbiota composition to metabolic and immune health and quality of life (determined by questionnaire)

Study design

Double-blind, placebo-controlled, randomized parallel design

Intervention

In this study there will be two different intervention groups:
1. Wheat-derived, Arabinoxylan-oligosaccharides (AXOS)
15g/day ingested with the meals (5 g in beverage, to be consumed three times a day)
2. Placebo/control: maltodextrin
15g/day ingested with the meals (5 g in beverage, to be consumed three times a day)

The duration of the intervention will be 12 weeks. The type of treatment will be blinded for both the volunteers and the researchers.

Study burden and risks

All subjects will be screened before participation and thereby receive information about their health status. The general interest of this study is to study effect of wheat bran-derived dietary fibers on intestinal health and functioning and metabolic health.
Burdens that volunteers can experience are the time spent with the study (subjects will have to invest approximately 30 hours in the study,divided among 2 test days, 2 screening visit and 4 short visits and the dietary and healthy regimen they have to follow. Also the collection of fecal samples can be experienced as a burden, because they have to handle them themselves and have to store them at home. Also the 12 week intake of the supplements can be seen as a burden for the subjects.
During the test days, blood will be collected via a venous catheter. Venapunctures can occasionally cause a local hematoma or a bruise. Some participants report pain during venapuncture. During visit 1, 40 ml blood will be taken. During visit 3 and 8 the total amount of blood sampled is 180 ml per test day, totaling 400 ml during the whole test period. During visit 3 and 8, an adipose tissue biopsy will be taken. The adipose tissue biopsy might cause local hematoma as well. To minimize the risk for a hematoma, the biopsy place will be compressed for approximately 10 minutes after biopsy. The place of incision will leave a small scar (3 mm for adipose tissue biopsy). To promote good wound healing, the incision will be sealed with sterile steristrips and a

waterproof band-aid.

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

- Healthy, normal/overweight men and women (BMI * 20 kg/m2 <30kg/m2)
- Aged 20-55 years
- Caucasian
- Normal fasting glucose (<6.1 mmol/L.)
- Normal blood pressure (systolic blood pressure 100-140 mmHg, diastolic blood pressure 60-90 mmHg)
- Weight stable in last 3 months (±2 kg)
- A low defecation frequency, <4 times/week and no constipation or underlying pathology

- A slow gastro-intestinal transit (> 50th percentile based on Sadik et al. 2003, 2004)

Exclusion criteria

- Woman lactating, pregnant or (post)-menopausal
- Regular smokers
- People with intensive fitness training, eg. athletes (*3 per week * 1 hour training)
- Diabetes Mellitus (defined as FPG * 7.0 mmol/l and or 2h PG * 11.1 mmol/l)
- Gastro-intestinal diseases or abdominal surgery, cardiovascular diseases, cancer, liver or kidney malfunctioning, disease with a life expectation shorter than 5 years.
- Following a hypocaloric diet
- Gluten intolerance
- Regular use of laxation products, or use of antibiotics, probiotics or prebiotics 3 months prior to the start of the study
- Current use of medication interfering with study intervention or interfering with study endpoints/hypotheses
- Not to be able to understand the study information
- Blood donation 2 months prior to the study and during the study
- Participation in other studies

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-09-2015
Enrollment:	52
Type:	Actual

Ethics review

Approved WMO Date:	24-06-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-09-2015
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-01-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 23115
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL52300.068.15
Other	study has been registered
OMON	NL-OMON23115

Study results

Date completed:	16-12-2016
Actual enrolment:	48