The effects of pectin on aging-related changes in intestinal barrier function, immune function and microbial composition

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

Summary

ID

NL-OMON42262

Source
ToetsingOnline

Brief title
Pectin, aging and intestinal barrier function

Condition

- Gastrointestinal conditions NEC

Synonym
Gastrointestinal symptoms

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Top Insitute of Food and Nutrition

Intervention

Keyword: Aging, Immune system, Intestinal barrier function, Pectin

Outcome measures

Primary outcome

Intestinal permeability

Gut permeability test in which the 24-hour urinary excretion of test substances (i.e. sucrose, lactulose, rhamnose, sucralose and erythritol) will be measured in two separate fractions (0-5 hours and 5-24 hours).

Measurement for intestinal permeability will take place at baseline and after the supplementation period of four weeks.

Secondary outcome

Intestinal barrier functioning:

• Tight junction structure and proteins in colonic biopies: immunofluorescent labelling and polymerase chain reaction (PCR) quantification of ZO-1, claudin-3 and occludin. Measurements of tight junction structure and proteins in colonic biopsies will take place only after the supplementation period of four weeks.

• Ussing chamber experiments in colonic biopsies: transepithelial electrical resistance (TEER), fluorescein- and horseradish peroxidase (HRP) flux. Ussing chamber experiments in colonic biopsies will take place only after the supplementation period of four weeks.

• Histology in colonic biopsies by staining mucus/mucins. Histologic assessment of colonic biopsies will take place only after the supplementation period of four weeks.

• MicroRNA 29a (MiR-29a) in colonic biopsies. Measurements of MiR-29a will take place only after the supplementation period of four weeks.

• Zonulin in blood plasma. Measurements of zonulin will take place at baseline and after the supplementation period of four weeks.

Immune system performance

• Immune cell infiltration by transcriptomics in colon biopsies. Measurements of immune cell infiltration will take place only after the supplementation period of four weeks.

• T-cells and natural killer cells (NK-cells) assessed in PBMC stimulated blood and measured by fluorescence-activated cell sorting (FACS). Measurements of T-cells and NK-cells will take place at baseline and after the supplementation period of four weeks.

• Mononuclear cells and platelets in blood plasma. Measurements of mononuclear cells and platelets will take place at baseline and after the supplementation period of four weeks.

• Cytokines and chemokines in 24h stimulated whole blood. Measurements of cytokines and chemokines will take place at baseline and after the supplementation period of four weeks.

• C-reactive protein (CRP) in blood serum. Measurements of CRP will take place at baseline and after the supplementation period of four weeks.

• Secretory Immunoglobulin A (sIgA) in blood serum, feces and saliva. Measurements of sIgA will take place at baseline and after the supplementation period of four weeks.

Microbial composition and -function

• Microbial composition in luminal content and feces as measured by Illumina sequencing. Measurements of microbial composition will take place at baseline and after the supplementation period of four weeks.

• Short-chain fatty acids in luminal content and feces as measured by high-performance liquid chromatography (HPLC). Measurements of short-chain fatty acids will take place at baseline and after the supplementation period of four weeks.

Metabolite production

• Volatile organic compounds in exhaled air as measured by gas chromatography time-of-flight mass spectrometry (GC-tof-MS). Measurements of volatile organic compounds will take place at baseline and after the supplementation period of four weeks.

Digestive parameters

• Symptom diary questionnaire. The symptom diary questionnaire will be completed three days prior to the supplementation period and three days during the last week of the supplementation period.

• Stool frequency and consistency (Bristol Stool Scale) questionnaire. The Bristol Stool Scale will be completed at baseline and every week during the supplementation period of four weeks.

• Gastrointestinal Symptom Rating Scale (GSRS) questionnaire. The GSRS will be completed at baseline and every week during the supplementation period of four

weeks.

Study description

Background summary

The intestines contain large amounts of bacteria which contribute to well functioning digestive system. Bacteria are involved in breakdown of nutrients, but also in the immune system of the human body. Previous research has been shown that dietary fibers are able to moduclate the composition of the microbiota, especially in the large intestine, thereby inducing additional health effects. In this study, we will investigate the effects of pecin, a dietary fiber which is naturally present in apple, citrusfruit and sugar beet, on intestinal barrier function. Further, we will investigate the the effects of pectin on microbial composition, degradition products and the immune system. In all these effects we are especially interested in the difference between healthy adults and healthy elderly.

Study objective

This study will be don to gain insights in the effects of the dietary fiber pectin on gut functioning and the immune system. The information will gain more insights in the working mechanism of this specific dietary fiber. Further, we are especially interested in possible different effects in healthy adults when compared to elderly people. In case study results will be positive, this may lead to the development of more and new health promoting foodproducts. In case there will be different effects in different age groups, this may lead to new foodproducts targeting one specific age group.

Study design

The study conforms to a randomized, double-blind and placebo-controlled design including two parallel arms

Intervention

Subjects will be randomized into one of the two groups. One group will receive 7.5 grams of pectin supplements twice daily for four weeks. A second group will receive 7.5 grams of placebo supplements twice daily for four weeks. Before and after the supplementation period, several measurements will take place.

Study burden and risks

There are several burdens volunteers can experience during this study. After the screening visit, participants will have to visit the Maastricht Universitair Medisch Centrum+ (MUMC+) four times. A participant will spend approximately eight hours at the university facility. They will have to take pectin or placebo supplements twice daily for a time period of four weeks; the supplements used have been proven to be safe for human use. During two visits, a total of 52 mL blood will be sampled by venepuncture via an evacuated tube system, which may lead to minor discomfort and/or a small hematoma at the site of puncture. During the same visits, saliva samples and exhaled air samples will be collected and subjects will bring a fecal sample which is collected at home. Furthermore, a gut permeability test will be performed twice for which subjects will have to ingest a sugar drink and will have to collect their urinary output for 24 hours and return this to the MUMC+. Moreover, questionnaires will have to be filled out at several occasions during this study. A subset of the participants will visit the MUMC+ for a fifth time to undergo a standard flexible sigmoidoscopy, during which biopsies will be taken and intestinal fluid contents will be sampled. These procedures bear a small risk (0.09%) of bowel perforation or bleeding at biopsy sites in general clinical use, however, the risk in the present study is expected to be much smaller, because instead of patients who undergo sigmoidoscopy for clinical reasons, healthy subjects without intestinal disease or other clinical indication will be investigated. A report of the *Gezondheidsraad* mentions a 0.0025% risk of perforation after screening for cancer in healthy subjects.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

No gastrointestinal complaints
Age between 18 - 40 years and 65 - 75 years
BMI between 20 and 30 kg/m2

Exclusion criteria

Use of PPIs, NSAIDs and/or vitamin supplementation, within 14 days prior to testing
Administration of probiotic or prebiotic supplements, investigational drugs or participation in any scientific intervention study which may interfere with this study in the 90 days prior to the study
Use of antibiotics in the 90 days prior to the study.
Pregnancy
Smoking

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-03-2015
Enrollment:	108
Type:	Actual

Ethics review

Approved WMO Date:	09-02-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-04-2015
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

No registrations found.

In other registers

Register	ID
CCMO	NL51235.068.14
Other	Volgt, registratie in clinicaltrials.gov