The effects of 2*-fucosyllactose and resistant starch on acetate production and human substrate metabolism

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Ethical review	Approved WMO
Status	Completed
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON55195

Source
ToetsingOnline

Brief title
2*-fucosyllactose and acetate production in vivo

Condition

- Diabetic complications
- Diabetic complications

Synonym
lipid metabolism, overweight

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: NWO CCC CarboKinetic

Intervention

Keyword: - 2□-fucosyllactose, - gut microbiota, - overweight, - short-chain fatty acids

Outcome measures

Primary outcome

Plasma and faecal acetate and other SCFA (ie. butyrate, propionate)

concentrations.

Secondary outcome

- Energy expenditure, fat and carbohydrate oxidation will be measured using an

open-circuit ventilated hood system (Omnical, Maastricht University, The

Netherlands);

- Circulating hormone concentrations (Insulin, GLP-1, PYY)

- Circulating metabolite concentrations (Glucose, Free Fatty Acids);

- Appetite (Visual Analog Scales (VAS)-scoring system for hunger and satiety).

- Breath H2 using (Bedfont EC60 Gastrolyzer, Rochester, UK).

- Faecal microbiota composition (16S RNA)

- Three-day food record.

A three-day food record will be completed three days prior to each CID.

- Gastrointestinal Symptom Rating Scale (GSRS) questionnaire.

Study description

Background summary

The gut microbiota is being increasingly recognized as an important factor in fat distribution, insulin sensitivity and glucose and lipid metabolism. Accordingly, the intestinal microbiota could play an important role in the development of obesity and diabetes. One of the important functions of the

human microbiota is the fermentation of indigestible carbohydrates, i.e. dietary fiber or resistant starches. The major products of this saccharolytic fermentation process are short-chain fatty acids (SCFA). Of note, several rodent in vivo studies showed that SCFA supplementation and enhanced SCFA production due to dietary fiber supplementation prevented diet-induced obesity and insulin resistance. We previously demonstrated in humans that the site of administration of SCFA is of major importance in humans. Here we concluded that increasing the availability of the SCFA acetate in the distal colon is necesssary to elicit beneficial effects on metabolic health. Furthermore, present literature suggests that the microbial acetate production and its metabolism differ between lean insulin sensitive and overweight/obese insulin resistant individuals.
Therefore, we hypothesize(1) that increasing the acetate availability in the distal colon will increase circulating acetate concentration and promote substrate and energy metabolism, and (2) that in a disturbed metabolic phenotype these effects are less pronounced, the following objective will be addressed:

Study objective

In one of our previous study we demonstrated that enhanced acetate availability in the distal, but not proximal, colon promote fat oxidation, energy expenditure and parameters of substrate and energy metabolism in healthy normoglycaemic men. In addition, present literature provides indication that acetate elicits differential effect on substrate and energy metabolism based on the metabolic phenotype.
Based on our hypothesis, which is (1) that increasing the acetate availability in the distal colon will increase circulating acetate concentration and promote substrate and energy metabolism, and (2) that in a disturbed metabolic phenotype these effects are less pronounced, the following objective will be addressed:
We will investigate effects of acute supplementation of 2-FL with and without resistant starch on faecal and blood plasma acetate availability and markers of substrate and energy metabolism during overnight fasted conditions and after a high-fat meal in two different metabolic phenotypes. We are interested in whether fiber supplementation leads to different SCFA production rates and consequent differences in metabolic outcomes in healthy, lean vs. overweight/obese, prediabetic individuals.

Study design

Double blind, placebo-controlled, randomized, crossover design.

Intervention

The day before each visit, participants consume one of the supplements with

standardized meals:
1. Placebo: 11.43 g (3 x 3.81 g) maltodextrin Glucidex IT 12 (Roquette Freres, Lestrem, France) (43.43 kcal/d)
2. 2-FL: 12 g (3 x 4 g) 2*-fucosyllactose (FrieslandCampina Domo, Netherlands) with 5.43.g (3 x 1.81 g) maltodextrin to make it isocaloric (43.43 kcal/d).
3. 2-FL + RS: 12 g (3 x 4 g) 2*-fucosyllactose (FrieslandCampina Domo, Netherlands) in combination with 9.375 g (3 x 3.125 g (80% resistant starch (3 x 2.5 g)) granular potato starch (Avebe, Veendam, The Netherlands) (43.43 kcal/d).

Study burden and risks

All participants will be screened before participation and thereby receive information about their health status. In the future there can be general health benefits for the public, but the volunteers will have no personal benefits by participating in the study. The general interest of this study is that there have never been human intervention studies investigating the supplementation of fermentable carbohydrate mixtures in different metabolic phenotypes and their effects on SCFA concentrations and on their substrate and energy metabolism. The amounts of 2-FL and resistant starch used in this study are previously used in several human trials and have been proved to be safe. In this study the volunteers may experience the following as a burden. After initial screening, subjects will have to invest approximately 18 hours in the study. During the study, blood will be collected via a venous catheter. Venepunctures can occasionally cause a local hematoma or bruise to occur. Some participants report pain during venepuncture. Also the collection of stool samples can be seen as a burden.

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

Twelve lean (BMI * 20kg/m2 and * 24.9kg/m2) healthy men aged 30 * 65 years and 12 overweight/obese (BMI * 25kg/m2 and * 34.9kg/m2) prediabetic men aged between 30 * 65 years.

Exclusion criteria

- Type 2 diabetes mellitus
- Gastroenterological diseases or abdominal surgery;
- Cardiovascular diseases, cancer, liver or kidney malfunction, disease with a life expectancy shorter than 5 years;
- Abuse of products; alcohol and drugs, excessive nicotine use defined as >20 cigarettes per day;
- Plans to lose weight or following of a hypocaloric diet;
- Regular supplementation of pre- or probiotic products, use of pre- or probiotics 3 months prior to the start of the study;
- Intensive exercise training more than three hours a week;
- Use of any medication that influences glucose or fat metabolism and inflammation (i.e. NSAIDs);
- Regular use of laxation products;
- Use of antibiotics in the last three months .

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	04-02-2020
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	18-12-2019
Application type:	First submission
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	NL71611.068.19