Butyrate/hexanoate-enriched triglycerides for metabolic health

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON49589

Source
ToetsingOnline

Brief title
Butyrate/hexanoate in metabolic health

Condition

- Appetite and general nutritional disorders

Synonym
obesity, overweight

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: AAK;the Netherlands

Intervention

Keyword: butyrate, hexanoate, metabolic health, short-chain fatty acids

Outcome measures

Primary outcome

Primary parameters:

The effects of acute supplementation of four different concentrations of

butyrate/hexanoate-enriched oil on plasma SCFA availability

Primary endpoint: Plasma SCFA concentrations.

Secondary outcome

- Circulating hormone concentrations (Insulin, GLP-1)

- Circulating metabolite concentrations (Glucose, Free Fatty Acids, Glycerol

and Triglycerides (TG));

- Circulating inflammatory markers (TNFα, IL1β, IL6 and IL8)

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

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

- Three-day food record. A three-day food record will be completed three days

prior to each clinical investigation day.

- 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 type 2 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), such as butyrate. Of note, several rodent in vivo studies showed that SCFA supplementation prevented diet-induced obesity and insulin resistance.

Even if the knowledge improved, in the present time, our understanding of the effects of SCFA on human metabolism is still limited. We previously performed acute studies where we administered SCFA in the colon of healthy, overweight men (METC 11-3-079, METC13-3-022). Our results demonstrated that an increase in circulating levels of SCFA are necessary to elicit beneficial effects on human substrate and energy metabolism. In another clinical trial, oral sodium butyrate intake resulted in improved insulin sensitivity in healthy adults and an improved anti-inflammatory response in adults with metabolic syndrome. However, the long-term effect of elevated intestinal and systemic butyrate concentrations on metabolic health has never been studied. Interestingly, hexanoate (also known as capronic acid, C6), another SCFA, can also be produced by the gut microbiota and is inversely associated with the inflammatory state. Therefore, a mixture of butyrate and hexanoate may be an interesting approach to combat obesity-associated chronic low-grade inflammation and tissue specific metabolic dysfunctions.

In this public-private partnership project, we aim to identify a well consumable butyrate/hexanoate-enriched oil that increases circulating SCFA concentrations and improves postprandial substrate metabolism, which could be further used for a long-term study.

Study objective

The objective of this project is to identify a well consumable butyrate/hexanoate-enriched oil that increase circulating SCFA levels and improves postprandial substrate metabolism.

We will investigate the effects of acute intake of four different concentrations of a butyrate/hexanoate-enriched oil (Akovita Postbiotics range) on plasma SCFA availability and markers of substrate and energy metabolism during postprandial conditions in overweight/obese men.

Study design

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

Intervention

During the clinical investigation day, participants will ingest a liquid high-fat mixed meal enriched with four different concentrations of a butyrate/hexanoate-enriched oil:
1. Placebo: 0 mg butyrate and hexanoate (10g high oleic sunflower oil (Fritex HOSO, AAK, The Netherlands))
2. 650 mg of butyrate and hexanoate (~8.6 g Akovita SCT-FAT8.5% and 1.4 g high oleic sunflower oil (AAK, The Netherlands))
3. 1325 mg of butyrate and hexanoate (~7.2 g Akovita SCT-FAT8.5%, 2.7 g Akovita SCT-FAT30%, and 0.1 g high oleic sunflower oil, (AAK, The Netherlands))
4. 2000 mg of butyrate and hexanoate (8.6g Akovita SCT-FAT30% and 1.4 g high oleic sunflower oil, (AAK, The Netherlands))

The type of intervention will be blinded for both the volunteers and the researchers and provided in randomized order.

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 is a great lack in well consumable SCFA enriched foods, which can be used for long term consumption to improve the control of body weight and insulin sensitivity.

The products used in this study are evaluated as safe for human use. All ingredients of the oil are regularly consumed in the form of i.e. food dairy products such as butter, ghee, raw milk, animal fats, fermented foods and food additives. In this study the volunteers may experience the following as a burden. After initial screening, subjects will have to invest approximately 28 hours in the study and have to fill in food diaries at home. During the clinical investigations days, 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.
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Overweight/obese men (BMI >= 25 kg/m2 and <= 34.9 kg/m2);
- Aged 40 - 70 years;
- Caucasian;
- Normal blood pressure (systolic blood pressure 100-140mmHg, diastolic blood pressure 60-90 mmHg);
- Weight stable for at least 3 months (± 2 kg).

Exclusion criteria

- Type 2 diabetes mellitus (defined as fasting plasma glucose >= 7.1 mmol/L)
- Gastroenterological diseases or abdominal surgery (gallbladder removal and appendix removal are allowed)
- Cardiovascular diseases, cancer, liver or kidney malfunction, disease with a life expectancy shorter than 5 years;
- Lactose intolerance or other disorders that affect digestion (such as celiac disease)
- Abuse of products; alcohol and drugs, excessive nicotine use defined as >20 cigarettes per day; and excessive alcohol use defined as (> 15 units/week)
- Plans to lose weight or following of a hypocaloric diet in the following three months;

- Regular supplementation of pre- or probiotic products (for example Yakult, Activia), 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. betablockers, corticosteroids, statins or NSAIDs);
- Regular use of laxation products in 3 months prior start of study or during study period;
- Use of antibiotics in the last three months (antibiotics use can alter substantially the gut microbiota composition).
- Follow a vegan diet or vegetarian diet.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-01-2021
Enrollment:	14
Type:	Actual

Ethics review

Approved WMO

Date:	13-11-2020
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	NL75253.068.20