# The effects of plant stanol esters on intestinal mucosal gene expression profiles and microbiota composition in healthy human subjects.

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Lipid metabolism disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON37742

**Source**
ToetsingOnline

**Brief title**
Plant stanols and gene expression profile

### Condition

- Lipid metabolism disorders

**Synonym**
Hypercholesterolemia

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universiteit Maastricht

**Source(s) of monetary or material Support:** RAISIO

## Intervention

**Keyword:** gene expression profiles, microbiota, plant stanols

## Outcome measures

### Primary outcome

Analysis of the intestinal mucosal gene expression profiles.

### Secondary outcome

Analysis of changes in microbiota composition.

Serum/plasma concentrations of plant sterols/stanols, lipids, lipoproteins,

free fatty acids, glucose, insuline and markers of endothelial dysfunction.

Analysis of the expression of nutrient sensing receptors (T1R2, T1R3,...)

# Study description

### Background summary

Plant sterols and stanols are components that are naturally present in plants. Their biological function in plants is comparable with these of cholesterol in animals. They are structurally related to cholesterol, but are absorbed by enterocytes to a much lesser extent. It is generally accepted that they inhibit intestinal cholesterol absorption and consequently lower serum low-density lipoprotein (LDL) cholesterol concentrations up to 10% at daily intakes of 2.5 g. The exact underlying mechanism of the plant sterol/stanol mediated reduction in intestinal cholesterol absorption is still unknown. It has been suggested that they lower the activity of sterol uptake transporters like Niemann-Pick C1 like 1 protein (NPC1L1) in enterocytes, otherwise several studies indicated that these compounds could activate the liver X receptor (LXR) in enterocytes, thereby activating the ABC transporters involved in the intestinal cholesterol metabolism, whereas recently suggestions have been made that plant sterols and stanols activate transintestinal cholesterol excretion (TICE). This is the

direct cholesterol secretion from the blood into the intestinal lumen, in which the enterocytes play a central role. None of these assumptions have so far been evaluated in humans.

## Study objective

The major objective of the present study is to examine the acute effects of dietary plant stanol esters on the intestinal mucosal gene expression profiles in intestinal biopsies in healthy volunteers. Two minor objectives are (1) to investigate whether semi-long-term use (3 weeks) of plant stanol esters have an effect on microbiota composition.

If the volunteers agree, we will take 2 extra jejunal biopsies. These will then be used as a control group to examine the expression of nutrient receptors.

## Study design

A randomized, double-blind, placebo-controlled cross-over design. The total study duration will be 12 weeks, consisting of 2 test periods of 4 weeks in which the volunteers will use a plant sterol/stanol poor diet for 1 week followed by the consumption of the investigational products for 3 weeks. Directly after the plant sterol/stanol poor diet period, at day one of the 3 weeks intervention period all volunteers will participate in a postprandial test. In this test volunteers will consume a meal with or without added plant stanol esters. Five hours after the breakfast meal with or without plant stanol esters, we will take a small intestinal biopsy to determine the acute changes in intestinal mucosal gene expression profiles. The day before the beginning of the plant sterol/stanol poor diet as well as during the last two days of the 3 week plant stanol ester or placebo consumption, we will sample stool for microbiota analysis.

## Intervention

During each test period, the volunteers will use a plant sterol/stanol poor diet for 1 week followed by the consumption of the investigational products (margarines with or without added plant stanol esters (3 g/day) for 3 weeks. During the 4-week wash-out period, they will return to their normal eating habits. For the postprandial tests at the start of the two experimental periods (week 2 and 10), the subjects will consume a high fat breakfast enriched with or without 4.0 gram plant stanols. Total follow-up during the postprandial period is 5.5 hours.

## Study burden and risks

Before the start of the study, subjects will be screened to determine eligibility. The study itself includes two times 1 postprandial test day;

duration of both days will be approximately 5.5 hours. On both days, subjects may not have any food or drinks other than water. During the postprandial test day, 8 blood samples and 8 intestinal biopsies will be taken, i.e. 4 duodenal and 4 in proximal jejunum.
Fasting blood samples will be drawn on 8 different occasions in a time frame of 12 weeks with a total amount of 139 mL. During the screening procedure, 2 mL blood will be sampled. Furthermore, subjects will be asked to fill out a food frequency questionnaire three times at the end of both experimental periods. Blood samples might cause bruises or haematoma. Obtaining small intestinal biopsies by standard flexible gastroscopy induces local discomfort in the pharynx only during the procedure, which takes about 15 minutes, and causes a theoretical risk for perforations (1:1000) and an infection risk of 1:1.800.000. Healthy subjects will have a lower risk.

## 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

aged between 18 and 60 years
Body Mass Index (BMI) between 20-30 kg/m2
mean serum total cholesterol < 7.8 mmol/L

### Exclusion criteria

unstable body weight (weight gain or loss > 3 kg in the past two months) - active cardiovascular diseases like congestive heart failure or recent (<6 months) event (acute myocardial infarction, cerebral vascular incident) - severe medical conditions that might interfere with the study such as epilepsy, asthma, chronic obstructive pulmonary disease, inflammatory bowel disease and rheumatoid arthritis) - indication for treatment with cholesterol-lowering drugs according to the Dutch Cholesterol Consensus - use of medication such as corticosteroids, diuretics or lipid lowering therapy - abuse of drug or alcohol (>21 units per week) - not willing to stop the consumption of vitamin supplements, fish oil capsules or products rich in sterol or stanol esters - use of an investigational product within another biomedical study within the previous month - pregnant or breast-feeding women - not willing to give up being a blood donor (or having donated blood) from 8 weeks before the start of the study and during the study - current smoker - anemia. with a Hb-level below 7.5 mmol/L for men and below 7.0 mmol/L for women, as indicated by the blood bank of Maastricht - gastrointestinal diseases - not willing to stop the consumption of probiotica and antibiotica during the study

## Study design

### Design

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

### Recruitment

NL
Recruitment status: Pending

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|---|---|
| Start date (anticipated): | 01-03-2012 |
| Enrollment: | 20 |
| Type: | Anticipated |

## Ethics review

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| Approved WMO Date: | 14-03-2012 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |
| Approved WMO Date: | 30-05-2012 |
| 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 |
|---|---|
| Other | - |
| CCMO | NL39197.068.12 |