# The PROFUN study: PROtein Fermentation UNraveled - Exploring the relationship between digestibility and metabolite production.

Published: 25-09-2023
Last updated: 19-10-2024

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Gastrointestinal signs and symptoms |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON56371

**Source**
ToetsingOnline

**Brief title**
PROFUN

### Condition

- Gastrointestinal signs and symptoms

**Synonym**
Protein fermentation

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Wageningen Universiteit

**Source(s) of monetary or material Support:** IMEC NL

## Intervention

**Keyword:** dietary protein, digestibility, fermentation, metabolites

## Outcome measures

### Primary outcome

Ammonia as biomarker for protein fermentation, measured in feces and urine and

in situ by the GISMO GEN1 ingestible.

### Secondary outcome

Secondary study parameters include other protein fermentation related

metabolites measured in feces, urine and blood; microbiome composition; transit

time; absorption kinetics.

# Study description

### Background summary

Protein intake is often higher than recommended in Western countries. This leads to increased amounts of protein flowing into the large intestine. Next to increased dietary protein intake, protein digestibility, and endogenous protein losses also affect the amount of protein entering the large intestine. However, these aspects have barely been studied, especially in humans. The large intestine is home to the largest bacterial ecosystem of the body. During the fermentation of protein by these bacteria (microbiota), metabolites are produced such as ammonia, branched-chain fatty acids, biogenic amines, phenolic compounds, indoles, and N-nitroso compounds. There is evidence that some of these metabolites could be harmful for gut epithelia, gastrointestinal health, and health in general after they enter blood circulation. In general, doing measurements inside the gastrointestinal tract is invasive. During this project we will study protein fermentation in the gastrointestinal tract using feces and urine, but also in situ using the GISMO GEN1 ingestible. This ingestible contains sensors to measure pH, ammonium, temperature, and redox potential.

### Study objective

The primary objectives of this study are:
1) To investigate the feasibility of the GISMO GEN1 System to monitor biomarkers in the gastrointestinal tract by studying the ingestible transit time, data coverage, participant experience, and serious adverse events (if applicable).
2) To study the effect of a 7-day high versus low digestible protein source present in the diet on protein fermentation in healthy subjects, measured by ammonia concentrations.

**Study design**

The study is divided into 2 phases.
In phase 1, preliminary feasibility of the GISMO GEN1 ingestible system will be assessed and the baseline measurements will be taken without any dietary restrictions. An interim analysis will be performed after phase 1 and only after a positive evaluation of the GISMO GEN1 System, the study will continue with phase 2.
Phase 2 is a randomized cross-over controlled feeding trial. Two diets will be used: one diet containing a high digestible protein source, and the other diet containing a low digestible protein source. Each diet will be given for 7 days, with a wash-out period in between. Measurements done during the dietary interventions will be compared to the other diet, and to the baseline measurements.

**Intervention**

A high digestible protein diet (30 g/d whey protein) and a low digestible protein diet (30 g/d bovine plasma protein).

**Study burden and risks**

This study is related to a broad general population. There are minor risks for the healthy research subjects of this study. The diets are composed by licensed dieticians of Wageningen University & Research. Subjects that participate in this study will invest approximately 31 hours in the study. They will visit the research facility 4 times: information and screening, baseline period, Test day during dietary intervention 1, and Test day during dietary intervention 2. The blood collection by a venous catheter for a half day during both diet interventions could be a burden and placement of the catheter could cause bruising. Participants will have to swallow 5 GISMO GEN1 ingestibles in total during the study. After taking the GISMO GEN1 ingestible, participants will have to collect all of their feces for several days to confirm the excretion of the capsule and to collect fecal samples for analyses.
If the ingestible is visible on the X-ray, 7 days later (14 days after administration) another X-ray is made. If the ingestible did not exit the GIT via feces after 14 days, a bowel cleanse with laxatives is advised. In the rare

case that a bowel cleanse did not lead to excretion of the ingestible, an endoscopic or surgical treatment is recommended depending on the location of the ingestible. The expenses for such treatments will be covered by the research team.
The participants do not directly benefit from the study but receive a financial compensation of ¤395,- after completing the study. Traveling expenditures will also be covered. Furthermore, all foods will be provided for 14 days during the intervention trial.

## 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

- Males and females
- Age between 16 years or older

- BMI between 18.5-30 kg/m2
- Normal bowel movement: at least one defecation per 48 hours
- Suitable veins for insertion of cannula

## Exclusion criteria

- Having a current or past medical history or surgical events that may either put the subject as risk because of participation in the study, or influence the results of the study, including, a swallowing disorder, gastrointestinal or liver or endocrine or renal or cardiovascular disease, any other chronic disease, partial bowel resection, renal failure, cancer, nose/throat diseases, gastric bypass surgery, use of anticoagulants; as determined by the medical supervisor;
- Use of any medications in the week before the study that could substantially alter gastrointestinal motor function (e.g., opioids, prokinetics, anticholinergics, laxatives), or acidity (PPI, H2RA), as determined by medical supervisor;
- Having a bleeding/coagulation disorder, including hemophilia, Von Willebrand disease, Bernard-Soulier, Glanzmann thrombasthenia or thrombocytopenia;
- Swallowing disorders; Among others: dysphagia, any oropharyngeal or oesophageal stricture, functional abnormality, or anxiety disorders related to swallowing disorders;
- Severe dysphagia to food or pills;
- Suspected or known strictures, fistulas, or physiological/mechanical GI obstruction;
- Previous GI abdominal surgery; Except: uncomplicated appendectomy, and/or laparoscopic cholecystectomy;
- Pregnancy, recent childbirth in last 6 months, or actively trying to get pregnant;
- Planned MRI procedure during the study;
- Pacemakers, defibrillator, infusion pump, or other implanted electromedical devices;
- Suffering >2 times per week from: nausea / vomiting / decreased appetite / abdominal pain / high blood pressure / headaches, shakiness, and weakness / fever / diarrhea / constipation;
- Unwilling to undergo an X-ray examination and/or ultrasound (in case sensorcapsule exit cannot be confirmed);
- Working in a professional healthcare facility (e.g. hospital, dental office, emergency room), military area (e.g. submarine, near radar installation), or heavy industrial area (e.g. power plants, automotive, mining, refineries) during the duration of the study;
- Having an allergy or intolerance towards compounds in the prescribed foods (e.g. gluten, lactose, fish, peanuts, soy, nuts);
- Following a vegetarian or vegan diet;
- Use of prebiotic supplements or probiotics for 3 months before the start of

the study;
- Use of antibiotics within 2 months of starting the study or planned during the study;
- Excessive alcohol consumption (alcohol: <21 consumptions/week for men, and <14 consumptions/week for women);
- Use of soft drugs within 1 month of starting the study or during the study;
- Use of hard drugs;
- Hemoglobin levels <8.5 mmol/L for men and <7.5 mmol/L for women;
- Participation in another biomedical study;
- Not having a GP;
- Being an employee of Wageningen University, Division of Human Nutrition and Health.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Crossover |
| Masking: | Double blinded (masking used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 10-10-2023 |
| Enrollment: | 15 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Generic name: | GISMO GEN1 System |
| Registration: | No |

# Ethics review

Approved WMO

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| Date: | 25-09-2023 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 | clinicaltrials.gov |
| CCMO | NL84483.091.23 |