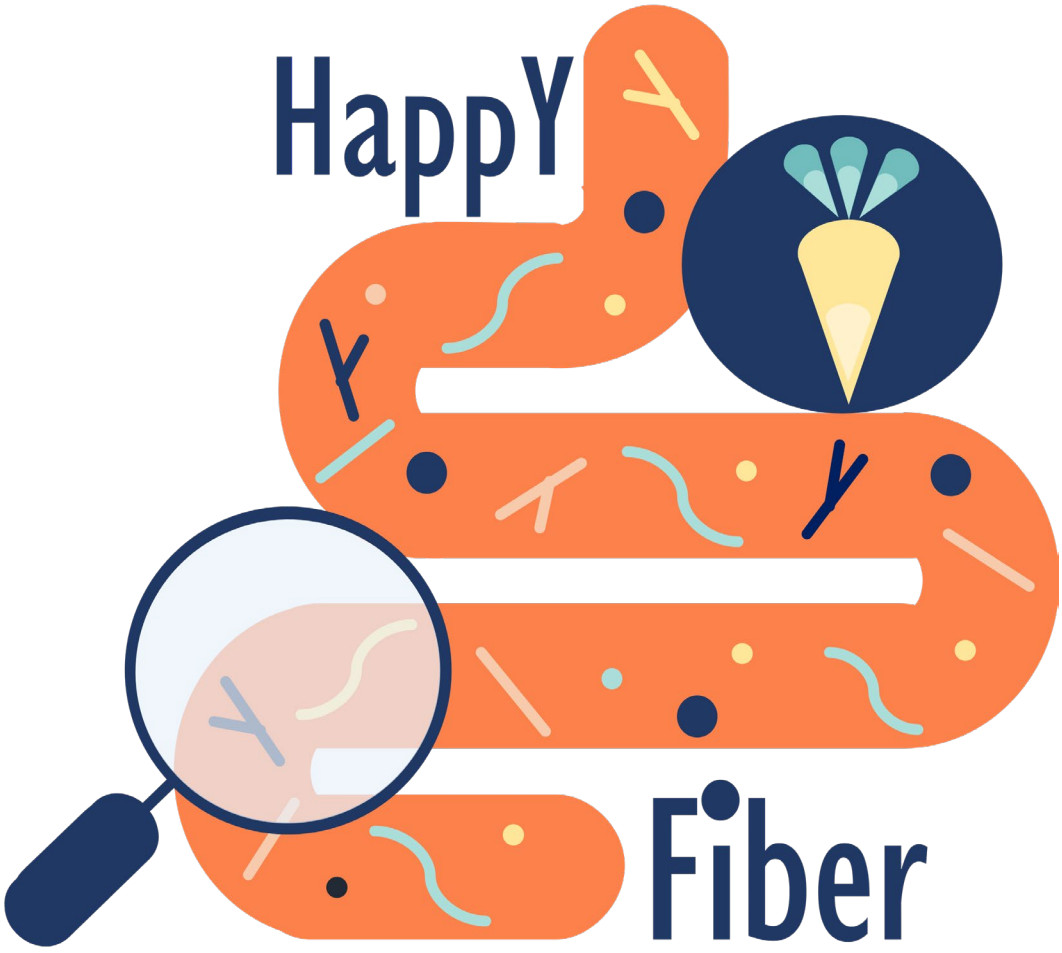
Subject information for participation in medical research

Impact of a dried vegetable on bowel function and gut bacteria

The impact of a dried vegetable on bowel function and gut microbiota in subjects with bowel function issues



Introduction

Dear Sir/Madam,

With this letter, we would like to ask you to take part in a medical study. Participation is voluntary. You have received this letter because you suffer from hard and infrequent bowel movements.
You can read about the medical study in this information sheet, what it means for you, and what the pros and cons are. It is a lot of information. Can you please read the information and decide if you want to take part? If you want to take part, complete the form in Appendix D.

Ask your questions

You can take your decision based on the information in this information sheet. We also suggest that you do this:
- Put your questions to the investigator who gave you this information.
- Talk to your partner, family or friends about this study.
- Ask questions to the independent expert, Dr Naguib Muhsen.
- Read the information on www.rijksoverheid.nl/mensenonderzoek.

1. General information

Wageningen University has set up this study. Below, we always call Wageningen University the 'sponsor'. Investigators, these can be investigators/research nurses, conduct the study in via the university.

This study needs 160 subjects. The Medical Ethics Review Committee METC Oost-Nederland has approved this study.

2. What is the purpose of the study?

In this study, we look at whether daily use of a dried, fibre-rich vegetable can change gut bacteria and bowel function in healthy subjects, who have suffer from hard and infrequent bowel movements.

3. What is the background of the study?

A healthy bowel function is essential for human wellbeing. Yet, a considerable number of people suffers from hard and infrequent bowel movements. People can experience this as, for instance, not going to the toilet often and having very hard stools. Altogether, this leads to dissatisfaction with one’s bowel function. Dietary fibre are essential for human health. You do not digest dietary fibre in your stomach, but they end up in your lower gut. In your lower gut you have bacteria, which digest these dietary fibre. By doing so, they produce small compounds, which we think are good for human health.

We believe that the type of bacteria you have in your gut influences your bowel function. But, we do not know exactly how they do that. At the same time, we do know that dietary fibre can change the type of gut bacteria. However, we do not know what role the amount of dietary fibre one consumes plays herein. That is why in this study we want to map the gut bacteria of people that have issues with their bowel function. And we want to look at how different amounts of dietary fibre can change the type of gut bacteria and bowel movements. As source of dietary fibre we use in this study a dried vegetable which comes from the roots of the Belgian endive (witloof) plant. This dried vegetable is very rich in dietary fibre and in an earlier study in people that had no bowel function issues, the use of this dried vegetable stimulated bowel function.

4. What happens during the study?

How long will the study take?
Are you taking part in the study? It will take about six weeks in total.

Step 1: are you eligible to take part?
First, we want to know if you are eligible to take part. That is the reason that the investigator is doing some checks:

- Questionnaire: First, we will first ask you a number of question regarding your general health, your gut health and your lifestyle.
- Bowel function diary: Second, we will ask you to keep a daily diary of your bowel movements for two weeks (how often you have bowel movements, how hard/soft the bowel movements are, if you have any bowel complaints etc).

You can participate in the study if:

- You are between 20 to 80 years old
- You are unsatisfied with your bowel function and/or you have between 1 to 4 bowel movements per week, which are most of the time hard, lumpy or solid
- You are able to speak and understand Dutch or English
- You have no history of medical or surgical events that may affect the study outcome, e.g. medically diagnosed irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD) or constipation
- You have not used antibiotics during the 3 months before the screening, and no use of laxatives during the screening, and no use of supplements containing fibers (other than laxatives), pro-/ post-/ synbiotics one month before the screening
- You are not a chronic user of antacids and PPI’s, and you do not use medication that lowers the blood sugar
- For women: You are not currently lactating or pregnant or planning to become pregnant
- You are not allergic to plants like lettuce, sage, tarragon, chamomile, Belgian endive (witloof), artichokes, daisies, sunflowers etc.
- You have no unexplained weight loss or weight gain of > 5 kg in the month before the screening and you do not follow a slimming or medically prescribed diet or macrobiotic life-style

- You have a general practitioner, you want te be informed about unexpected discoveries in relation to your health and you are able to follow the study procedures
- You do not work at the Division of Human Nutrition & Health or the Laboratory of Microbiology of Wageningen University

Please note: it is possible that you are not eligible for this study, even if you are healthy. The investigator will tell you more about this.

Step 2: the use of the dried vegetable
You will use the dried vegetable for four weeks.
For this study, we will have 4 groups that differ in the daily amount (dosage) of the dried vegetable:

- Group 1. The people in this group will get the highest dosage dried vegetable.
- Group 2. The people in this group will get the medium dosage dried vegetable.
- Group 3. The people in this group will get the lowest dosage dried vegetable.
- Group 4. The people in this group will a control consisting of a dried food (for comparison).

A draw will decide which amount dried vegetable you are given. You and the investigator do not know which group you are in. But if it is important for your health, we can look this up.

Step 3: study and measurements
For the study, you need to keep track of your bowel movements for four weeks and you need to collect five stool samples. Moreover, for this research it is needed that you participate in two (online) meetings. Depending on the COVID-19 regulations these meetings can be at Wageningen university or online. Both meetings will take about 30 to 60 minutes.
We will carry out these checks during the research:

- Stool sample test. For this, you will collect weekly a stool sample (so one sample per week). In total, you will collect five stool samples. With these stool samples, we test these things:
    - Which type of bacteria you have in your gut.
    - Which compounds your gut bacteria produce.
- You fill in questionnaires/diaries.
    - A diary of your bowel movements. You fill this in daily. It takes about 5 minutes every day.
    - A questionnaire about how satisfied you are with your bowel function and how much problems you had with your bowel function. And a questionnaire about your habitual physical activity. You fill in these questionnaires twice, once at the begin of the study and once at the end of the study. It takes you about 35 minutes to fill-in these questionnaires.
    - A diary for three days about what you eat. You fill in this diary once at the begin of the study and once at the end of the study. It takes you about 30 minutes on each of these three days to fill in this diary.

- Optional: Consumption of blue muffins – this a method to measure the time food needs to travel through your gut (transit time). For this method muffins are eaten that are coloured blue with a food dye. The food dye is approved by the EU for consumption (E122/E133) and badly taken up from your intestine and ends up in your faeces. We provide these muffins. If you are interested herein, you will eat two blue muffins; once during the screening and once during the last week of the study. You record the time and day when you eat the muffins. And you record the time and day the blue food dye appears in your bowel movements. As you already monitor your bowel movements with a diary, this measurement does not take you extra time. But you decide whether you want to do this measurement or not.

Appendix C has an overview of the measurements we carry out and how much time they take during the screening and during the study.

5. What agreements do we make with you?

We want the study to go well. That is why we want to make the following agreements with you:

- You take the dried vegetable and fill in the diaries/questionnaires in the way the investigator explained to you.
- You do not change your diet or the amount of physical activity during the study.
- You do not take part in any other medical research during this study.
- You come to every (online) appointment.
- You should contact the investigator in these situations:
    - You want to start taking other medication. Also, if these are homoeopathic remedies, natural remedies, vitamins or over-the-counter medicines.
    - You are hospitalised or get treatment in a hospital.
    - You suddenly have problems with your health.
    - You no longer want to take part in the study.
    - Your telephone number, address or email address changes.

The following text is only relevant for women

Pregnancy and lactating during the study?

Women who are pregnant or breastfeeding cannot take part in this study. This is due to the hormonal changes temporarily affecting bowel function. If you do become pregnant during the study, please inform the investigator. In this case, you will discuss with the investigator when to stop participating in the study.

6. What side effects, adverse effects or discomforts could you experience?

The dried vegetable may cause side effects.

Please note: notify the investigator immediately if you experience:
- You cannot have bowel movements at all
- Your bowel function issues worsen
- Other unexpected causes

The following side effects are common:
- Flatulence, bloating, rumbling

It may help to spread the amount of dried vegetable over the day, to drink sufficiently, to not wear tight clothing and to maintain your normal lifestyle (dietary habits and physical activity). Often the side-effects cease after some days.

7. What are the pros and cons if you take part in the study?

Taking part in the study can have pros and cons. We will list them below. Think about this carefully and talk to other people about it.

The dried vegetable may have beneficial effects on your gut bacteria and bowel function, but that is not certain. But if you take part you will help the investigators to get more insight into the functioning of gut bacteria in subjects that have issues with their bowel function and the potential relief thereof. We can also give you insight into the type of gut bacteria you have.

Taking part in the study can have these cons:
- You may experience the side effects or adverse effects of an increased consumption of dietary fibres due to the dried vegetable, as described in Section 6.
- Taking part in the study will cost you extra time. You have to monitor your bowel movements daily using the diary (5min) and you have to collect five times a stool sample. At the begin and end of the study you have to take note of what you eat for three days (30 min per day) and you have to fill in two questionnaires (30 min). Finally, you have to participate in two (online) sessions (30-60 min).
- You have to comply with the study agreements.

You do not wish to participate in the study?
It is up to you to decide if you wish to participate in the study. You do not wish to participate? Your doctor can tell you more about the available options for treatment. And about the pros and cons.

8. When does the study end?

The investigator will let you know if there is any new information about the study that is important to you. The investigator will then ask you if you want to continue to take part.

In these situations, the study will stop for you:

- All checks according to the schedule are finished.
- The end of the whole study has been reached.
- You have become pregnant.
- You want to stop participating in the study yourself. You can stop at any time. Report this to the investigator immediately. You do not have to explain why you want to stop. You can then discuss with your doctor whether you wish to pursue a standard treatment for bowel function issues. The investigator will still invite you for a follow-up check.
- The investigator thinks it is better for you to stop. The investigator will still invite you for a follow-up check.
- One of the following authorities decides that the study should stop:
    - Wageningen University,
    - the government, or
    - the Medical Ethics Review Committee assessing the study

What happens if you stop participating in the study?
The investigators use the data and body material (stool samples) that have been collected up to the moment that you decide to stop participating in the study. If you wish, we will destroy the collected body material. Please let the investigator know.

The entire study ends when all the participants have finished.

9. What happens after the study has ended?

Will you get the results of the study?
About half a year after you took part in the study, the investigator will inform you about the most important results of the study. The investigator may also tell you what group you were in. Do You prefer not to know? Please tell the investigator. He will not tell you in that case.

10. What will be done with your data and body material?

Are you taking part in the study? Then you also give your consent to collect, use and store Your data and body material.

What data do we store?
We store these data
- Your name
- Your gender

- Your address
- Your date of birth
- information about your health
- (medical) information that we collect during the study

What body material do we store?
We store stool samples.

Why do we collect, use and store your data and body material?
We collect, use and store your data and your body material to answer the questions of this study. And to be able to publish the results.

How do we protect your privacy?
To protect your privacy, we give a code to your data and your body material. We only put this code on your data and body material. We keep the key to the code in a safe place in the research centre. When we process your data and body material, we always use only that code. Even in reports and publications about the study, nobody will be able to see that it was about you.

Who can see your data?
Some people can see your name and other personal information without a code. These are people checking whether the investigators are carrying out the study properly and reliably. These persons can access your data:

- National and international supervisory authorities. For example, the Healthcare and Youth Inspectorate.

These people will keep your information confidential. We ask you to give permission for this access.

For how long do we store your data and body material?
We store your data in the research centre for 15 years. We store your body materials in the research centre. They will be stored for 15 years in order to be able to make new assessments related to this study in the course of this study. If no longer needed, we will destroy your body material.

Can we use your data and body material for other research?
Your data and your (remaining) body material may also be important after this study for other medical research on gut bacteria and gut health. For this purpose, your data and body material will be stored in the research centre for 15 years. Please indicate in the consent form whether you agree with this.

What happens if there are accidental discoveries?

It is possible that during the study we discover something that is important to your health. In that case, the investigator will contact you and then forward you to your doctor. You will then discuss what needs to be done with your doctor or specialist.

Can you take back your consent for the use of your data?
You can take back your consent for the use of your data at any time. This applies both to the use in this study and to the use in other medical research. But please note: if you take back your consent, and the investigators have already collected data for research, they are still allowed to use this information. The investigators will destroy your body material after you take back your consent. But if assessments with your body material have been carried out, the investigator can continue to use the results.

Do you want to know more about your privacy?

- Do you want to know more about your rights when processing personal data? Visit www.autoriteitpersoonsgegevens.nl.
- Do you have questions about your rights? Or do you have a complaint about the processing of your personal data? Please contact the person who is responsible for processing your personal data. For the present, this is:
    - Wageningen University: See Appendix A for contact details, and website.
- If you have any complaints about the processing of your personal data, we recommend that you first discuss them with the research team. You can also contact the Data Protection Officer of Wageningen University. Or you can submit a complaint to the Dutch Data Protection Authority.

Where can you find more information about the study?
You can find more information about the study on the following website (s): www.ClinicalTrials.gov and/or www.clinicaltrialsregister.eu. After the study, the website may show a summary of the results of this study. You can find the study by searching for 'Impact of a Dried Vegetable on Bowel Function and Gut Microbiota' (number: NCT05473793).

11. Will you receive compensation if you participate in the study?

You will get an expense allowance of € 120 for taking part in this study. If after the two weeks keeping the bowel movements diary, you are not eligible to participate int he study, you will receive a voucher of € 20. You will also be paid for eventual extra travel expenses (€ 0,19/km), if you live outside a radius of 10 km. If you stop before the study is finished, the compensation you receive will be less. The compensation for taking part in this study is declared to the Tax and Customs Administration as income.

12. Are you insured during the study?

Insurance has been taken out for everyone who takes part in this study. The insurance pays for damage caused by the study. But not for all damage. You can find more information about this insurance and any exceptions in **Appendix B**. It also says who you can report damage to.

13. We will not inform your doctor.

The investigator will not inform your doctor to let them know that you are taking part in the study. However, if we unexpectedly discover something during the study that is important for your health we may forward you to your doctor.

14. Do you have any questions?

You can ask questions about the study to the research team. Would you like to get advice from someone who is independent from the study? Then contact Dr Naguib Muhsen. He knows a lot about the study, but is not a part of this study.
Do you have a complaint? Discuss it with the investigator. If You prefer not to do so, please contact the complaints officer. Appendix A tells you where to find this.

15. How do you give consent for the study?

You can first think carefully about this study. Then you tell the investigator if you understand the information and if you want to take part or not. We wait until a week after the information session before we contact you again. If you want to take part, fill in the consent form that you can find with this information sheet. You and the investigator will both get a signed version of this consent form.

Thank you for your attention.

16. Appendices to this information

A. Contact details of Wageningen University
B. Information about the insurance .
C. Overview of the study interventions.
D. Consent form(s)

Appendix A: contact details for Wageningen University

Investigator:
Marie-Luise Puhlmann, MSc
Wageningen University
Helix Building
Stippeneng 4, 6708 WE Wageningen
T: 0638031129
E: marie-luise.puhlmann@wur.nl
Availability: Monday to Friday 9:00 – 18:00

Independent professional:
Dr Naguib Muhsen, MD, MFPM
Willem Baerdesenstraat 4
1067 XX Amsterdam
T: 020 354 7777 / 0616963517
E: nmuhsen@hotmail.com

Complaints officer:
Eveline Waterham
Afdeling Humane Voeding, Wageningen University
Helix gebouw 124
Stippeneng 4
6708 WE Wageningen
E: eveline.waterham@wur.nl
Availability: Mo, Tue, Thu, Fri 9:00 – 17:00

Data Protection Officer of the institution:
Dhr. Frans Pingen
Privacy@wur.nl

For more information about your rights: https://autoriteitpersoonsgegevens.nl/nl

Appendix B: information about the insurance

Wageningen University has taken out insurance for everyone who takes part in the study. The insurance pays for the damage you have suffered because you participated in the study. This concerns damage you suffer during the study or within 4 years after the study has ended. You must report damage to the insurer within 4 years.

Have you suffered damage as a result of the study? Please report this to this insurer:

The insurer of the study is:	
Name:	HDI- Global SE, the Netherlands
Address:	Westblaak 14, 3012 KL Rotterdam
Telephone number:	+31(0) 10 40 36 100
Website:	www.hdi.global
Policy number:	V-055-862-396-3 / V0100109572

The insurance pays a maximum of €650,000 per person and €5,000,000 for the entire study (and € 7,500,000> per year for all studies by the same sponsor).

Please note that the insurance does **not** cover the following damage:

- Damage due to a risk about which we have given you information in this sheet. But this does not apply if the risk turned out to be greater than we previously thought. Or if the risk was very unlikely.
- Damage to your health that would also have happened if you had not taken part in the study.
- Damage that happens because you did not follow directions or instructions or did not follow them properly.
- Damage to the health of your children or grandchildren.
- Damage caused by a treatment method that already exists. Or by research into a treatment method that already exists.

These provisions can be found in the 'Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015' ('Medical Research (Human Subjects) Compulsory Insurance Decree 2015'). This decision can be found in the Government Law Gazette (https://wetten.overheid.nl).

Appendix C: Description of study interventions

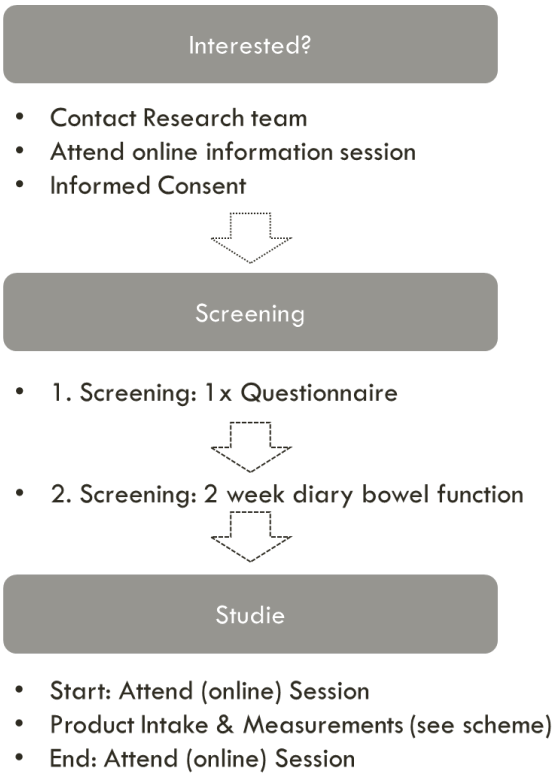


Figure 1 Overview of study

	Screening		Study				
			Week 1				
Measurements	Week 1	Week 2	before staring product intake	after staring product intake	Week 2	Week 3	Week 4
Study product intake				Daily	Daily	Daily	Daily
Diary bowel movement	Daily	Daily		Daily	Daily	Daily	Daily
Stool sample*			1x	1x	1x	1x	1x
Questionnaires: bowel function satisfaction & symptoms, habitual physical activity			1x				1x
Diary food intake			3 days				3 days
*Blue Muffins consumption***	1x						1x

* sending the stool collection kit and the retning of the stool samples will be arranged together with you
** this is an optional measurement (you may choose to do or not do this)

Figure 2 Overview of measurements in the study

Appendix D Informed consent form – subject

Belonging to **Impact of a dried vegetable on bowel function and gut microbiota**

- I have read the information sheet. I was able to ask questions. My questions have been answered well enough. I had enough time to decide if I wanted to take part.
- I know that taking part is voluntary. I also know that at any time I can decide not to take part in the study. Or to stop taking part. I do not have to explain why.
- I give consent to collect and use my data and body material. The investigators only do this to answer the question of this study.
- I know that some people will be able to see all of my data to review the study. These people are mentioned in this information sheet. I give consent to let them see my data for this review.
- For women: I know that I need to stop if I pregnant during the study.

- Please tick yes or no in the table below.

I give consent to store my data to use for other research, as stated in the information sheet.	Yes ☐	No☐
I give consent to have my (remaining) body material stored for use in other research, as stated in the information sheet. The body material is stored for this purpose for another 15 years.	Yes ☐	No☐
I give consent to ask me after this study if I want to participate in a follow-up study.	Yes ☐	No☐
I give consent to let me know after the study which treatment I received/in which group I was.	Yes ☐	No☐
I want to be informed about unexpected discoveries in relation to my health.	Yes ☐	No☐
I want to participate in the blue muffin gut transit time method.	Yes ☐	No☐

- I want to take part in this study.

My name is (subject): ……..
Signature: …… Date : __/__/__

I declare that I have fully informed this subject about the study mentioned.

If any information becomes known during the study that could influence the subject's consent, I will let this subject know in good time.

Investigator name (or their representative): .....
Signature:…… Date: __/__/__

The study subject will receive a complete information sheet, together with a signed version of the consent form.