

# Effect of probiotics on the intestinal microbiota of healthy adults

<b>Submission date</b> 11/03/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 29/07/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 10/03/2016	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Probiotics, or friendly bacteria, are live bacteria and yeasts that some consider to have a number of various health benefits. They are often eaten in yoghurts or taken as food supplements. They have been taken by people on antibiotics in order to prevent antibiotic-associated diarrhoea. Antibiotics can destroy the protective bacteria in the gut, leading to the aforementioned diarrhoea; high doses of certain probiotics can help restore the balance of gut bacteria and prevent the condition. However, the benefits to healthy people taking probiotics is difficult to measure. The aim of the PROBIOTA study is to assess the effects of taking a probiotic on the balance of gut bacteria in healthy people.

### Who can participate?

Healthy adults, aged between 18 and 55.

### What does the study involve?

Participants are initially asked to follow their normal diet for four weeks, with the only restriction being to not eat food containing probiotics (such as probiotic yoghurts). After this, each participant is randomly allocated to one of two groups. Those in group 1 are given probiotic capsules. Group 2 are given a placebo. The capsules are taken, preferably with water, twice a day for another four weeks. This is followed by a four week washout period, where all participants resume their normal diet (excluding probiotics). The participants in group 2 are then given the probiotic for four weeks, and group 1 the placebo. Fecal samples are collected from each participant before and after each treatment to test for gut bacteria.

### What are the possible benefits and risks of participating?

The benefits and risks of this trial are those conventionally associated with eating commercial probiotic products and are considered low.

### Where is the study run from?

The Department of Food, Environmental and Nutritional Sciences, University of Milan (Italy)

### When is the study starting and how long is it expected to run for?

February 2013 to May 2014

Who is funding the study?

The study is partially financed by a research grant from the Cariplo Foundation (Milano, Italy) and partly by a research collaboration fund stipulated between Università degli Studi di Milano and Sofar S.p.A (Italy)

Who is the main contact?

Dr. Simone Guglielmetti

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## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Protocol serial number

N/A

## Study information

### Scientific Title

Effect of the consumption of probiotic microorganisms on the composition and activity of the fecal microbiota of healthy adults

### Acronym

PROBIOTA

### Study objectives

The intestinal microbiota exerts a number of activities on human physiology. The modulation of the intestinal microbiota is therefore proposed to have effects on human health. Probiotics are believed to affect the composition of the intestinal microbiota, but such modifications have been never carefully defined for the healthy population. The use of high throughput sequencing technology in metagenomics may serve to properly describe the potential modifications induced by a probiotic dietary intervention of intestinal microbiota.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Ethics Committee of the University of Milan, 19/12/2012, ref: 37/12

**Study design**

Randomized double-blind placebo-controlled crossover study

**Primary study design**

Interventional

**Study type(s)**

Other

**Health condition(s) or problem(s) studied**

N/A

**Interventions**

Current interventions as of 30/10/2015:

The trial consists of four phases:

1. Pretreatment (4 weeks)
2. First treatment (4 weeks)
3. Washout (4 weeks)
4. Second treatment (4 weeks)

The trial includes five visits per participant:

1. Before pretreatment (visit V0)
2. Before the first treatment (i.e. after the pretreatment) (V1)
3. After the first treatment (i.e. before the washout) (V2)
4. Before the second treatment (i.e. after the washout) (V3)
5. After the second treatment (V4).

During a pre-recruitment phase (4 weeks), volunteers will follow their conventional diet with the only prohibition to consume: probiotic fermented milk (traditional yogurt is allowed), probiotic food formulas, foods enriched in prebiotic molecules, prebiotic food formulas. At the end of the pre-recruitment stage, volunteers will be randomized to receive the one probiotic formulation or placebo for 4 weeks. Probiotic formulations are two: (i) Enterolactis® Plus constituted by capsules containing at least 24 billion CFU (colony forming units) of freeze-dried *Lactobacillus paracasei* DG; (ii) Bb probiotic, constituted by capsules containing at least 1 billion CFU (colony forming units) of freeze-dried *Bifidobacterium bifidum* Bb. The placebo will be constituted by capsules with identical dimensions, color and taste to the probiotic product. The capsules will be consumed with water in the morning (preferably) at least 10 minutes before breakfast or in the evening at least 2 hours after the last meal of the day. After the 4-week treatment, a 4-week wash-out period will follow. After the wash-out, volunteers will receive the probiotic or placebo capsules for 4 weeks, according to the cross-over design.

One fecal sample is collected from each participant at V1, V2, V3, and V4. Every fecal samples is prepared for analysis of the microbiota and the quantification of microbial metabolites. Specifically, the microbiota of fecal samples will be characterized by Ion Torrent PGM sequencing of 16S rRNA-based amplicons obtained using the primer pair Probio\_Uni and

/Probio\_Rev, which encompass the V3 hypervariable region of the 16s rRNA gene. Analyses of microbial metabolites in feces will be performed by high performance liquid chromatography (HPLC; for the quantification of short chain fatty acids) and ultra performance liquid chromatography - tandem mass spectrometer (UPLC-MS/MS; for the quantification of primary and secondary bile salts).

Previous interventions:

The trial consists of four phases:

1. Pretreatment (4 weeks)
2. First treatment (4 weeks)
3. Washout (4 weeks)
4. Second treatment (4 weeks)

The trial includes five visits per participant:

1. Before pretreatment (visit V0)
2. Before the first treatment (i.e. after the pretreatment) (V1)
3. After the first treatment (i.e. before the washout) (V2)
4. Before the second treatment (i.e. after the washout) (V3)
5. After the second treatment (V4).

During a pre-recruitment phase (4 weeks), volunteers will follow their conventional diet with the only prohibition to consume: probiotic fermented milk (traditional yogurt is allowed), probiotic food formulas, foods enriched in prebiotic molecules, prebiotic food formulas. At the end of the pre-recruitment stage, volunteers will be randomized to receive the probiotic formulation or placebo for 4 weeks. Enterolactis® Plus will be constituted by capsules containing at least 24 billion CFU (colony forming units) of freeze-dried *Lactobacillus paracasei* DG. The placebo will be constituted by capsules with identical dimensions, color and taste to the probiotic product. The capsules will be consumed with water in the morning (preferably) at least 10 minutes before breakfast or in the evening at least 2 hours after the last meal of the day. After the 4-week treatment, a 4-week wash-out period will follow. After the wash-out, volunteers will receive the probiotic or placebo capsules for 4 weeks, according to the cross-over design.

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## **Intervention Type**

Other

## **Phase**

Not Applicable

## **Primary outcome(s)**

Assessment of the ability of the probiotic to modify the fecal microbiota in healthy adults (as determined by 16S rRNA gene metagenomic profiling). All outcomes are assessed at V1, V2, V3, and V4.

**Key secondary outcome(s)**

1. Change in bowel habit
2. Change in fecal metabolite concentration (e.g., short chain fatty acids, bile salts)
3. Persistence of probiotic microorganism in the intestine of volunteers

All outcomes are assessed at V1, V2, V3, and V4.

**Completion date**

01/05/2014

**Eligibility****Key inclusion criteria**

1. Healthy male or female subjects, aged between 18 and 55 years
2. Signed study-specific informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Antibiotic therapy during one month before the first visit
2. Viral or bacterial enteritis during the two months before the first visit
3. Gastric or duodenal ulcers during the five years before the first visit
4. Pregnant or breastfeeding women
5. Recent or presumed episodes of alcoholism or drug addiction
6. Presence of conditions determining a non-conformity of the volunteer to the study protocol

**Date of first enrolment**

01/02/2013

**Date of final enrolment**

01/05/2014

**Locations**

## **Countries of recruitment**

Italy

## **Study participating centre**

**Università degli Studi di Milano**

Department of Food, Environmental and Nutritional Sciences (DeFENS)

Division of Food Microbiology and Bioprocessing

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## **Sponsor information**

### **Organisation**

DeFENS - Division of Food Microbiology and Bioprocessing (Italy)

## **Funder(s)**

### **Funder type**

Research organisation

### **Funder Name**

The Cariplo Foundation (Italy), research grant 2010-0678

### **Funder Name**

Università degli Studi di Milano (Italy)

### **Funder Name**

Sofar S.p.A (Italy)

## **Results and Publications**

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/11/2014		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes