Bioactives Lead to Enhanced Disease defence

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON21522

Source
Nationaal Trial Register

Brief title
MiBlend

Health condition

Chronic diseases: cancer, cardiovascular disease, type II diabetes

Sponsors and support

Primary sponsor: Maastricht University
Source(s) of monetary or material Support: MiFood

Intervention

Outcome measures

Primary outcome

- The level of oxidative DNA damage in ex-vivo treated lymphocytes:lymphocytes will be challenged ex-vivo to hydrogen peroxide which is able to generate oxygen radicals. These oxygen radicals are known to be able to damage our DNA, either by means of directly inducing strand breaks or by means of adduct formation. The amount of DNA strand breaks in the DNA can be measured by means of the alkaline Comet assay;

- The level of oxidative stress parameters: To evaluate the effect of the different intervention on the level of oxidative stress, the antioxidant capacity of blood plasma will be measured by means of the Trolox Equivalent Antioxidant Capacity (TEAC) assay, and the levels of ROS will be measured by electron spin resonance (ESR). Furthermore, the level of excretion of 8-iso-prostaglandin F2 in urine as marker for lipid peroxidation will be measure;
- Cardiovascular risk parameter: changes in microcirculation. A promising new biomarker for cardiovascular disease risk is a change in the retinal microvasculature. Therefore, diameters of retinal vessels will be measured in a photographed image of the fundus of the right eye in order to produce summary indices representing the mean retinal arteriole calibre (CRAE) and mean retinal venule calibre (CRVE).
- Whole genome gene expression analyses. In order to gain more insight into the molecular mechanisms, whole genome gene expression analyses will be carried out in whole blood using 1-color microarray analyses (Agilent 8 × 60 K Whole Human Genome microarrays).
- Evaluation of the prevalence of different polymorphisms. In order to evaluate whether subgroups with different genetic characteristics respond differently on the consumption of different MiFood products the impact of different polymorphisms related to disease risk (cancer, diabetes type II, cardiovascular disease) and metabolisms of bioactive compounds on the different phenotypic markers and gene expression changes will be established.

Secondary outcome

- Bioavailability of different phytochemicals in the different interventions, plasma levels of e.g. vitamin C, quercetine, alpha-carotene, beta-carotene, lutein, lycopene, resveratrol, alpha-tocopherol, cryptoxanthin, glucosinulates, and total polyphenols will be measured by means of high-performance liquid chromatography (HPLC).
- Composition of the different white blood cells by means of a white blood cell count.
- OPTIONAL Phenotypical markers:In case the study identifies processes on gene expression level related to lipid metabolism, immune response and/or glucose homeostasis, additional measurements of phenotypic markers will be carried which are associated with the identified biological processes and include e.g.:
- The level of different plasma lipid levels such as cholesterol by measuring total cholesterol, high density lipoproteins (HDL), and low density lipoproteins (LDL), and triglycerides using standard kits;
- The level of plasma homocysteine by means of ELISA;
- Platelet activation by measuring platelet factor 4 and P-selectin in plasma using ELISA;
- Immune response markers, like TNF-alpha, interleukin-6, and C-reactive protein, using ELISA;
- The level of fasting glucose and insulin levels in plasma in order to quantify insulin resistance and beta-cell function by means of Homeostatic model assessment (HOMA model).

Study description

Background summary

Rationale:
People who eat sufficient amounts of fruits and vegetables as part of their daily diet have a reduced risk of a number of chronic diseases, such as cancer, cardiovascular disease and type II diabetes mellitus. There is ample scientific evidence suggesting that these health benefits are the consequence of the combined action of different phytochemicals present in fruits and vegetables. However, the number of studies in humans is limited. More research is needed to unravel the most optimal combination of phytochemicals in fruits and vegetables that can protect against disease risk. Furthermore, the underlying mechanisms by these phytochemicals exert their effect remain unclear. In addition, people might respond differently to dietary changes due to their genetic make-up. It was shown that subjects with specific genetic characteristics may benefit more from certain combinations of phytochemicals than others. More combinations of fruits and vegetables should be tested in humans with different genetic characteristics at the level of appropriate phenotypic markers of effect, including whole genome gene expression changes in order to provide insight into the underlying molecular mechanisms. Therefore, the aim of the present human dietary intervention study is to evaluate the effect of various combinations of vegetables and fruit containing different complex mixtures of phytochemicals in healthy volunteers on the level of phenotypic markers of disease risk in combination with whole genome gene expression analyses, and taking genetic variability, based on a selection of genotypes, between subjects into account.

Objective:
The main objective of the human dietary intervention study is to investigate the beneficial health effects of food products containing various combinations of an equivalent of 400 grams vegetables and fruits in healthy volunteers. This will be evaluated in different subgroups with specific genetic characteristics on the level of different phenotypical markers, combined with gene expression profiling.

Study design:
This human dietary intervention study has a randomized controlled cross-over – repeated measures design, including only healthy volunteers. After a two week run-in period, subjects will be randomized into one of the 9 study groups. Each group will follow two intervention periods of two weeks in which at each period one of nine different food product containing different combinations of vegetables and fruits will be consumed, separated by a one week washout period. At baseline and after each intervention period, blood and urine is collected, and a photograph is taken from the fundus of the right eye for analyses of markers of oxidative stress, DNA damage, biomarkers of cardiovascular disease risk and type II diabetes, gene expression analyses and determination of genetic polymorphisms.

Study population:
All subjects will be recruited at the University of Maastricht (UM) in the province of Limburg, the Netherlands, using advertisements, flyers as well as other (social) media. Healthy subjects of both sexes will be selected based on predefined inclusion criteria (BMI: 18-27; 18-60 years of age) and exclusion criteria, and randomly assigned to one of the different experimental groups.

Intervention:

Nine different food products containing different combination of fruits and vegetables will be evaluated in this human dietary intervention study. Seven of these 9 different food products consist of a smoothie, containing 400 grams of vegetables and fruits which will be consumed during the day: Smoothies 1-4 contain a specific selection of vegetables and fruit resulting in an overrepresentation of a specific class of phytochemicals. Smoothies 5-7 will consist of a combination of the four different classes overrepresented in smoothies 1-4, with increasing biodiversity. Food product 8 and 9 will consist of a pearl which is a crouton-like product, consisting of a core of oats, and will be either coated or non-coated with the most diverse mixture of vegetables and fruits as used in smoothie number 7. Each subject will be randomized into one of the nine study groups, which will start of a two week run-in period followed by two intervention periods of two weeks separated by a washout-period. At each intervention period, one of the nine different food products will be consumed. At baseline, and after each intervention period, blood and urine will be collected, as well as a photographic image of the fundus of the right eye will be taken.

Main study parameters/endpoints:
- To measure differences at the level of different phenotypic markers of disease risk: oxidative DNA damage in ex-vivo treated lymphocytes, antioxidant capacity of blood plasma, reactive oxygen species levels in blood, excretion of lipid peroxidation products in urine, plasma levels of different markers for cardiovascular disease and type II diabetes, and changes in the retinal microvasculature.
- To measure whole genome gene expression analyses in order to provide more insight in to the underlying molecular mechanisms. Genes and involved molecular processes associated with the measured phenotypic markers will demonstrate a causal relationship between the particular intervention and the markers of disease risk.
- To measure the occurrence of different polymorphisms related to disease risk in order to identify particular subgroups that will benefit more from a particular intervention.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Healthy volunteers will have to sign an informed consent and must follow a strict diet in consultation with a dietician. The food products contain different combination of vegetables and fruits, at the level of recommendations, which are freely available and are considered to be healthy. Participants will have to come to the university 8 times. The first visit only comprises signing of the informed consent and oral explanation of the study design by the principle investigator. At baseline, and after the first and second intervention period, subjects will come to the university after an overnight fast and donate urine and blood. Also a photograph of the fundus of the right eye is taken. In total, subjects will have to collect three times 24 hour urine, at 3 times 34 mL of blood divided over 4 vacutainers will be drawn, and 3 images of the fundus of the right eye will be taken. The other visits will be used for picking up of the food products. The risk of collection of these samples is considered to be minimal. During the whole study period, subjects have to keep track of their diet using a food diary.

Study objective

We hypothesize that consumption of mixtures of 400 grams vegetables and/or fruits for 2 weeks will result in lower ex-vivo induced oxidative DNA damage, increased antioxidant

capacity of blood plasma, reduced levels of reactive oxygen species in whole blood, reduced excretion of 8-iso-prostaglandin F2 in urine, changes in microcirculation I.e. wider retinal arterioles and narrower venules, and changes in the expression of genes in such a way that the involved molecular processes will be positively modulated thereby contributing to prevention of chronic disease risk.
We hypothesize that subgroups with different genetic characteristics based on a selection of genotypes, respond differently to the intervention by establishing the impact of different polymorphisms related to disease risk (cancer, diabetes type II, cardiovascular disease) and metabolisms of bioactive compounds.

Study design

There are three timepoints:
1) pre-test: after two week run-in period
2) post-test 1: after the first intervention period of two weeks
3) post-test 2: after the second intervention period of two weeks

Intervention

A dietary intervention study will be performed to establish the beneficial health effects of 9 different food products, produced by MiFood (a company involved in food production industry (www.mifood.nl)), containing various combinations of phytochemicals from different combinations of vegetables and fruits. Seven of these 9 different food products will consist of a smoothie, containing different combinations of vegetables and fruits. Smoothies 1-4 will contain a specific selection of vegetables and fruit resulting in an overrepresentation of a specific class of phytochemicals. Smoothies 5-7 will consist of a combination of the four different classes overrepresented in smoothies 1-4, with increasing botanical diversity. The remaining two dietary interventions will test a crouton (also called pearl), consisting of a core of oats and rice flour, either coated or non-coated with the most diverse mixture of vegetables and fruits as used in dietary intervention number 7.

Contacts

Public
Maastricht University
Simone van Breda

0031433882127
Scientific
Maastricht University
Simone van Breda

0031433882127

Eligibility criteria

Inclusion criteria

- Healthy men or women with a Body Mass Index (BMI) between 18.5 and 27;
- Between 18-60 years old.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Alcohol abuse up to 6 months before participation in this research, i.e. more than 4 drinks on any single day and more than 14 drinks per week for men and more than 3 drinks on any single day and more than 7 drinks per week for women;
- Current presence of any diseases related to the gastrointestinal tract, kidney, liver, heart or lungs;
- Current presence of type I or type II diabetes;
- Current presence of symptoms related to diseases of the gastrointestinal tract, i.e. vomiting, diarrhea or constipation, and altered stool, such as blood in stool;
- Current presence of diseases related to the endocrine or metabolic system;
- Current presence of anemia;
- HIV infection or hepatitis;
- Use of antibiotics and other medication (except contraceptives) over the last 3 months;
- Use of dietary supplements during the 3 months before start of the study;
- Known allergies for fruits and/or vegetables
- Known allergies for oats and/or rice flour
- Current smokers and ex-smokers who stopped during the 3 months before start of the study;
- Vegetarians and vegans;
- Pregnant women;
- Sportsmen and sportswomen who are physically active for more than 8 hours per week
- Participants of other intervention studies during this intervention period.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2019
Enrollment:	200
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion

Date:	15-04-2020
Application type:	First submission

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
NTR-new	NL8532
Other	METC azM/UM : METC 18-008

Study results

Summary results
No publications yet