Effect of AN-PEP enzyme on gastrointestinal breakdown of immunogenic gluten epitopes in healthy subjects

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Primary: • Assess effect of AN-PEP on gluten epitope degradation in the duodenumSecondary: • Assess effect of AN-PEP on gluten epitope degradation in the stomach• Assess effect of meal caloric content on the efficacy of AN-PEP on gluten epitope...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON35905

Source
ToetsingOnline

Brief title
AN-PEP-02

Condition

- Gastrointestinal inflammatory conditions
- Food intolerance syndromes

Synonym
celiac disease, gluten intolerance

Research involving
Human

Sponsors and support

Primary sponsor: DSM Food Specialties
Source(s) of monetary or material Support: DSM Food Specialties B.V.

Intervention

Keyword: celiac disease, digestion, enzyme, gluten

Outcome measures

Primary outcome

Effect AN-PEP with a low or high caloric meal on duodenal gluten epitope

exposure

Secondary outcome

Effect AN-PEP with a low or high caloric meal on

gastric gluten epitope concentrations and AUC over time

gastric and duodenal pH

gastric half emptying time

gastric and duodenal epitope concentrations or absolute amounts over

time related to 3 and 4

Difference in means between a low and high caloric meal with AN-PEP in all

endpoints mentioned above

Study description

Background summary

Celiac disease is an autoimmune disorder of the small intestine that occurs in genetically predisposed people. Celiac disease is caused by an immune reaction to gluten protein found in wheat, barley and rye. The immune system cross-reacts with the small-bowel tissue, causing an inflammatory reaction, particularly in the distal duodenum. That leads to a truncating of the villi

lining the small intestine and mal-absorption of nutrients. The only available treatment is a lifelong gluten-free diet.
The gluten epitopes that are responsible for the immune reaction, are rich in proline. The DSM enzyme AN-PEP (Apergillus Niger Prolyl EndoProtease) specifically cleaves gluten epitopes by cleaving behind these proline-residues. In vitro, AN-PEP was shown to effectively degrade gluten epitopes into non-immunogenic fragments under gastrointestinal conditions. It remains to be demonstrated in vivo to what extent and how fast AN-PEP can degrade gluten epitopes in the stomach and, how much remaining epitopes enter the small intestine. A second question is whether the caloric density of a meal can influence the efficacy of AN-PEP to degrade gluten by delaying gastric emptying and hence prolonging meal residence time.

Study objective

Primary:
• Assess effect of AN-PEP on gluten epitope degradation in the duodenum
Secondary:
• Assess effect of AN-PEP on gluten epitope degradation in the stomach
• Assess effect of meal caloric content on the efficacy of AN-PEP on gluten epitope degradation in the stomach and duodenum

Study design

A randomized, double-blind, placebo-controlled cross-over study in healthy subjects (n=12 completers).

Intervention

All subjects will come to the study site for 4 test days with one week in between. At test days, a gastro-duodenal catheter will be placed in the stomach and duodenum under x-ray control. Subsequently, subjects randomly receive, in a cross-over fashion, one of the 4 following meals:
1. A low caloric gluten meal together with AN-PEP drink
2. A high caloric gluten meal together with AN-PEP drink
3. A low caloric gluten meal together with placebo drink
4. A high caloric gluten meal together with placebo drink
Meals (300 mL) contain fat, carbohydrate and 5.2 g of gluten powder (4 g gluten protein).
Paracetamol is added to the meals to measure gastric emptying rate. The dilution maker polyethylene glycol-3350 (PEG3350) will be continuously perfused into the duodenum using the feeding catheter. PEG-3350 will be analyzed in all intraduodenal samples, to determine the dilution of the samples with endogenous gastrointestinal secretions.
During the 60 minutes prior to administration of the meal and during the 240 minutes thereafter fluid samples from the stomach and small intestine will be

taken through the feeding tube. Blood samples will also be collected.

Study burden and risks

None. There is a theoretical risk of creating a perforation during insertion of a feeding tube. There is no literature on the magnitude of this risk. The risk of placing a feeding tube in healthy volunteers is considered as nil.
Participants will experience mild discomfort during the insertion of the tube. The placement is done under X-ray screening. The total radiation exposure is minimal, estimated to be 0.20 mSv. This is equal to the amount of radiation that the body is exposed to during a flight of 3 hours at 4 km altitude (www.nrg-nl.com).
During blood sampling, a total amount of 44 ml blood will be taken per test day. In total, 176 ml blood will be obtained from each subject during this study. No side effects are to be expected, except from the possible occurrence of a bruise on the site of blood sampling. This will disappear within a few days.

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

Healthy;
Age >=18 but <45 yr
women; hormonal contraceptive therapy

Exclusion criteria

Any medical condition that may interfere with the study and may jeopardise the health status of the participant
women; no use of hormonal contraceptive therapy

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2011
Enrollment:	17
Type:	Actual

Ethics review

Approved WMO Date:	25-07-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-11-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC 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
ClinicalTrials.gov	NCT01335503
CCMO	NL36447.068.11