Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

The role of cereal grain related constituents and ingredients in human health

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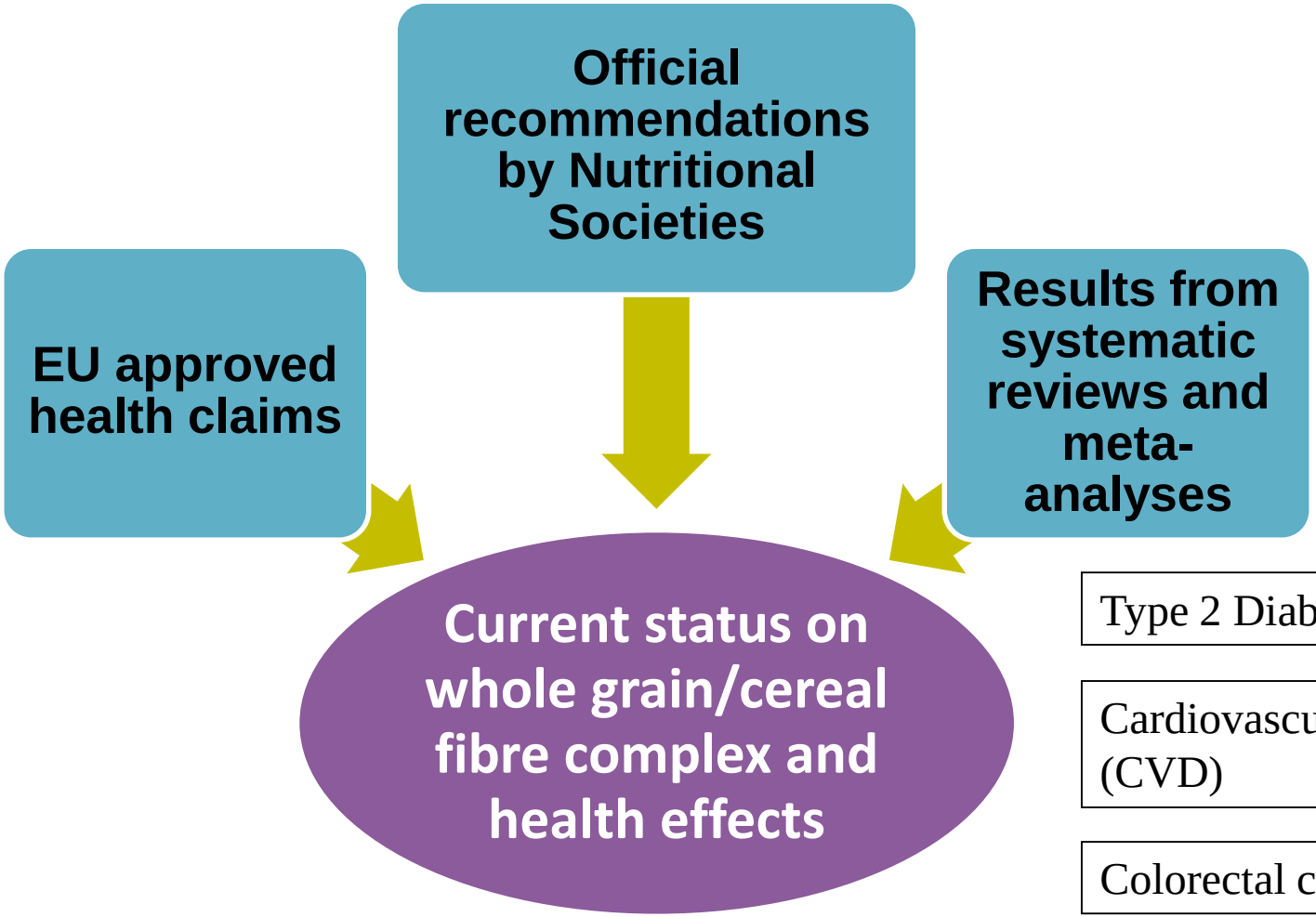
2016-08-29

Cereals
What are the evidences for impact on health?

Health effects of cereal foods



- Type 2 Diabetes (T2D)
- Cardiovascular disease (CVD)
- Colorectal cancer (CRC)

Whole grain, dietary fibre, and cardiometabolic disease– meta analysis

The Journal of Nutrition
Nutritional Epidemiology

Greater Whole-Grain Intake Is Associated with Lower Risk of Type 2 Diabetes, Cardiovascular Disease, and Weight Gain[1–3]

Eva Qing Ye,[4–6,9] Sara A. Chacko,[4–6,9] Elizabeth L. Chou,[4–6] Matthew Kugizaki,[8] and Simin Liu[4–7]*

- Review and meta-analysis of 45 prospective cohorts and 21 randomized intervention trials indicates that ***increased intake of whole grain*** and ***fibre may lower the risk of T2D, CVD, and weight gain.***

- ***Highest vs lowest cereal fibre intake was associated with a 16% and 19% lower risk of developing T2D and CVD, respectively.***

- Long-term RCTs seem warranted to elucidate mechanisms underlying the potential beneficial effects for the prevention of chronic diseases.

Ye et al. J Nutr. 2012 Jul;142(7):1304-13.

Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies

Subsite	No. of case patients/control subjects	IRR(95%CI)
Colorectal cancer	1372/1372	
Scandinavia	448/448	
Central Europe	517/517	
The Mediterranean	407/407	
Rectal cancer	501/501	
Scandinavia	196/196	
Central Europe	183/183	
The Mediterranean	122/122	
Colon cancer	871/871	
Scandinavia	252/252	
Central Europe	334/334	
The Mediterranean	285/285	
Proximal colon cancer	367/367	
Scandinavia	98/98	
Central Europe	164/164	
The Mediterranean	105/105	
Distal colon cancer	427/427	
Scandinavia	139/139	
Central Europe	145/145	
The Mediterranean	143/143	

Kryo et al. J Natl Cancer Inst;2014;106:1–9

Health Claims and whole grain evaluated by EFSA

- *Whole grain **is not** sufficiently characterized in relation to claimed effects- cause effect relationship cannot be established*

Effects:

- gut health/bowel function
- weight control
- blood glucose/insulin levels
- weight management
- blood cholesterol
- Satiety
- glycaemic index
- digestive function and cardiovascular health

*Whole grains are **defined differently** AND whole grains **are different***

EFSA Panel on Dietetic Products, Nutrition and Allergies (2010). Scientific Opinion on the substantiation of health claims related to whole grain. EFSA Journal 8(10):1766 (16 pp.).

Whole grain health claims Approved by US FDA

In 1999:

"Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol, may help reduce the risk ***of heart disease*** and ***certain cancers*** "

http://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm073639.htm &
http://www.fda.gov/Food/IngredientsPackagingLabeling/LabelingNutrition/ucm073634.htm

In 2013:

"Whole grains may reduce the risk of ***type 2 diabetes***, *although the FDA has concluded that there is very limited scientific evidence for this claim*."

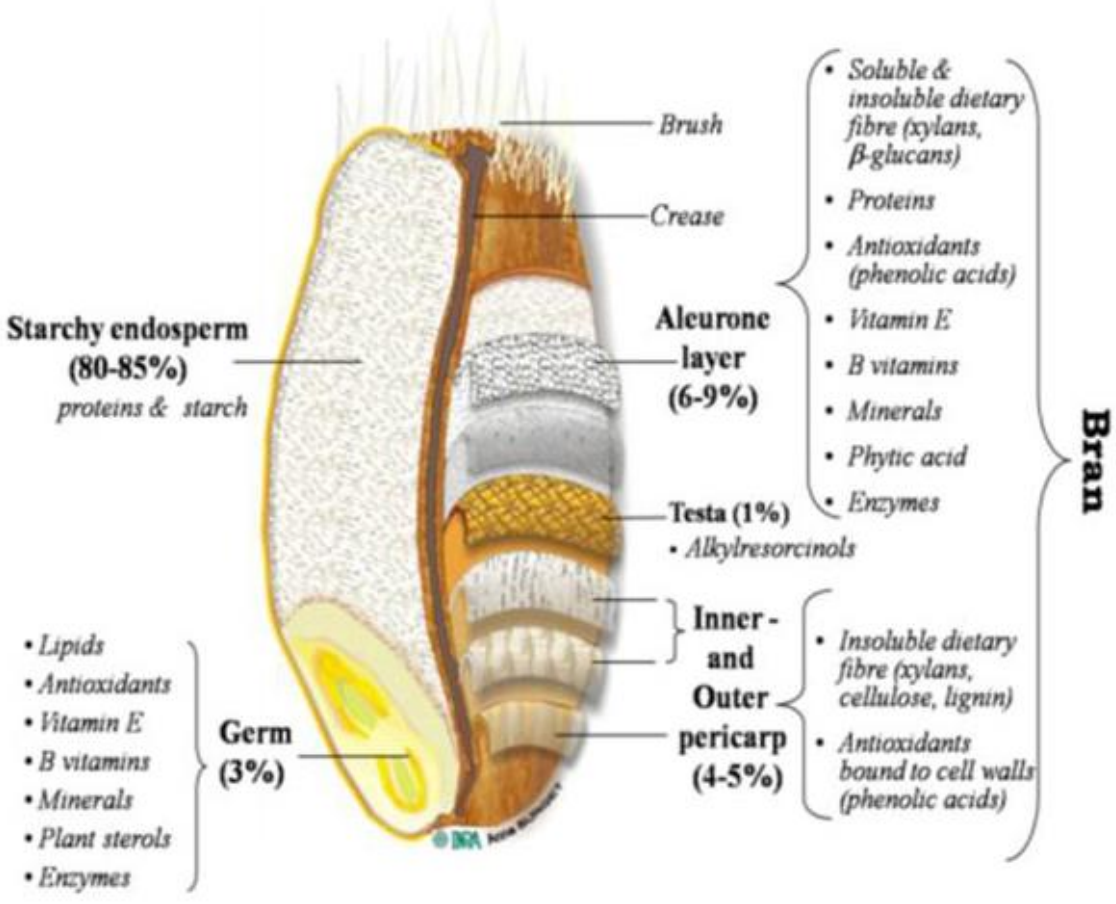
…but nutrition societies and authorities recommend a high whole grain intake!

”Chose whole grain whenever you eat bread, flakes, pasta or rice” www.slv.se

What in grains may provide health benefits?

- The kernel has 3 major parts:
  - Bran
  - Germ
  - Starchy Endosperm
- Whole grain flour contains 100% of the original germ and bran
- Bran and germ have a high content of fibre, micronutrients (vitamins, minerals, trace-elements) and bioactive plant compounds (antioxidants, sterols, etc).

The wheat grain kernel and its components:

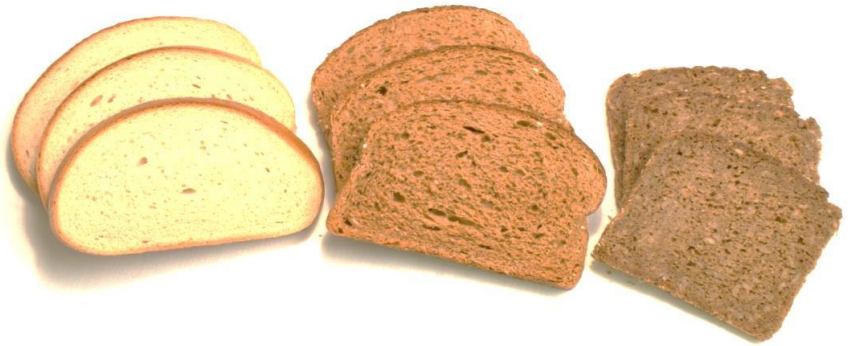


Source: Surget A, Barron C. Histologie du grain blé. Industries des Céreales. 2005; 145:3-7.

Grains AND grain fractions are different!

Dietary fibre (g/100g DM)

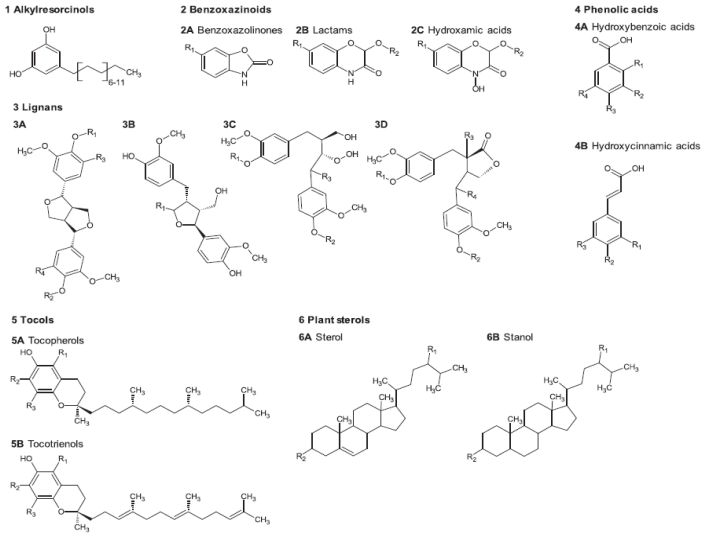
Fraction	Wheat	Oats	Rye	Rice	Maize
Whole grain	12	11	15 (20)	4	7
Bran	43	15	44 #	21	79
Starchy endosperm	2.7	6.5	8	2	1.9
Germ	13		-	-	-



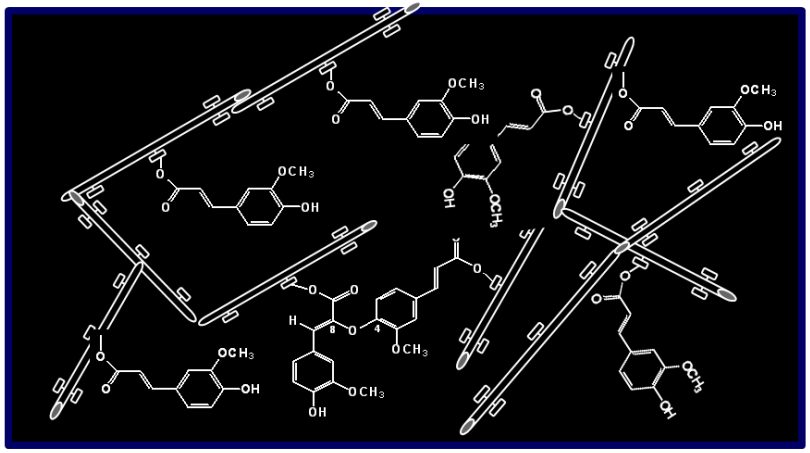
Data provided from USDA National Nutrient Database for Standard Reference. Cereal grains fiber content (available 2013-04-25). http://ndb.nal.usda.gov/ndb/search/list
#Kamal-Eldin et al. (2009) Food Nutr Res.

Examples of free and bound phytochemicals in grains

Free



Bound



Hydrocinnamic acids such as ferulic, p-comaric and sinapic acids and their dimers are present to greater extent in cereals (mainly bound) than in fruits and vegetables. (Neacsu et al. (2013) *Food Chemistry*)

Compound	Wheat (µg/100g)	Rye (µg/100g)
Tocols	28-80	44-67
Phenolic acids (90-95% bound)	326-1171	491-1082
Plant sterols	670-960	1098-1420
Alkylresorcinols	241-677	797-1231
Lignans	3.4-23	25-67
Benzoxazinoids	4.8	95

CODEX - FIBRE DEFINITION (2008/09)

Dietary fibre[1] means carbohydrate polymers with 10 or more monomeric units[2], which are not hydrolysed by the endogenous enzymes in the small intestine of humans and belong to the following categories:

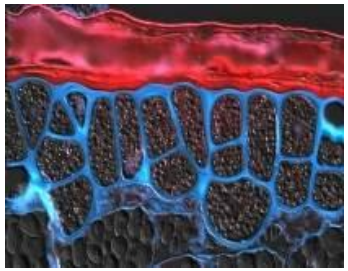
- Edible carbohydrate polymers naturally occurring in the food as consumed

AND

- Carbohydrate polymers, which have been obtained from food raw material by physical, enzymatic or chemical means

- Synthetic carbohydrate polymers

which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities.



1) Dietary fibre may include fractions of lignin and/or other compounds when associated with polysaccharides in the plant cell walls (full text of definition:see explanation below)

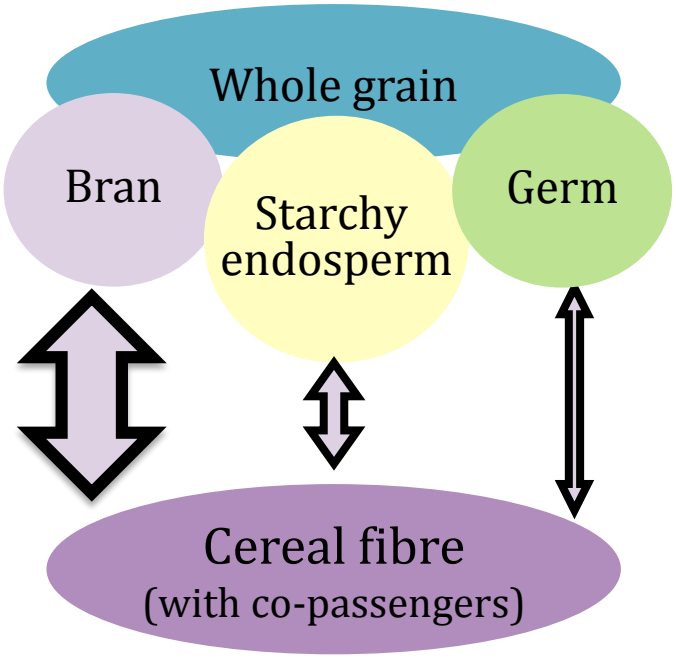
2) Decision on whether to include carbohydrates from 3 to 9 monomeric units should be left to national authorities

Note: oligosaccharides DP 3 – 9 included by EU and many others e.g. Canada, China, Japan

Cereal fibre in the Codex-classification system

Codex definition of fibre → **Synthesized fibre**

Fibre naturally occurring in foods



Isolated fibre

From grain kernels:

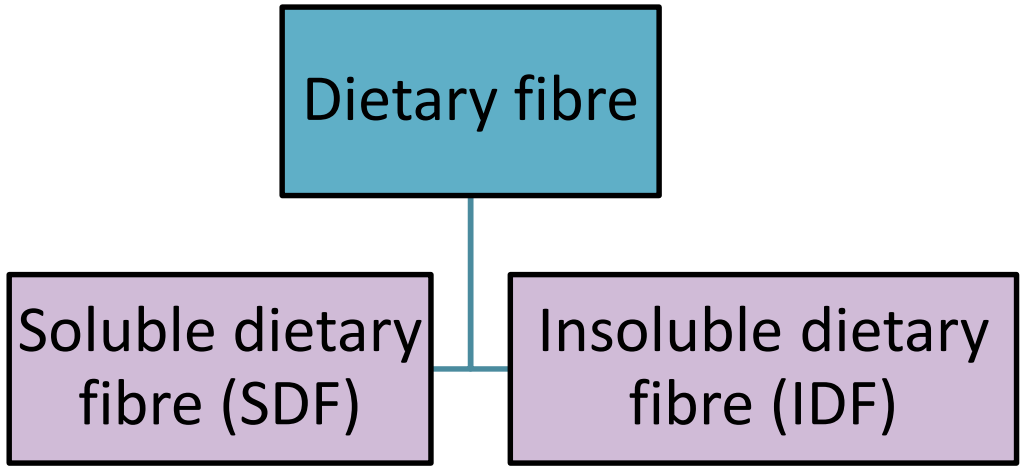
- Soluble arabinoxylan from wheat endosperm
- Resistant maltodextrin from wheat
- Resistant starch from maize

From straw, or husks:

- Cellulosic fibres

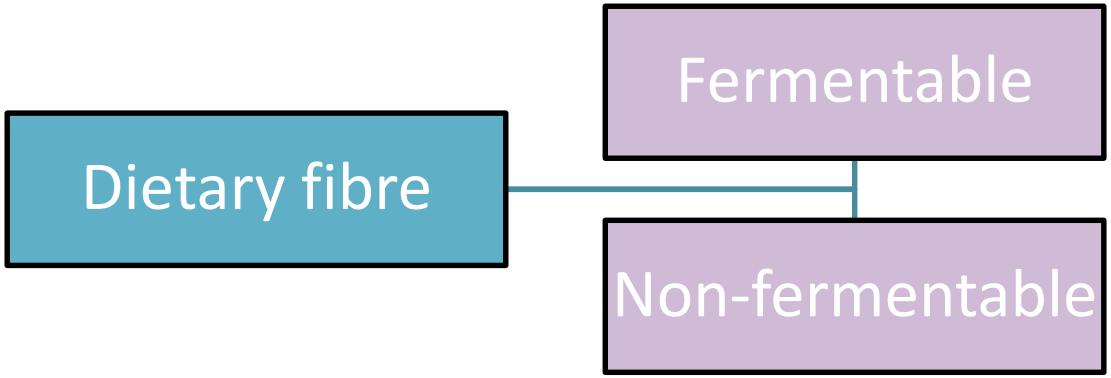
Isolated fibre
purified, (often) without co-passengers

Other classification systems



AOAC Method 991.43 measures SDF and IDF separately

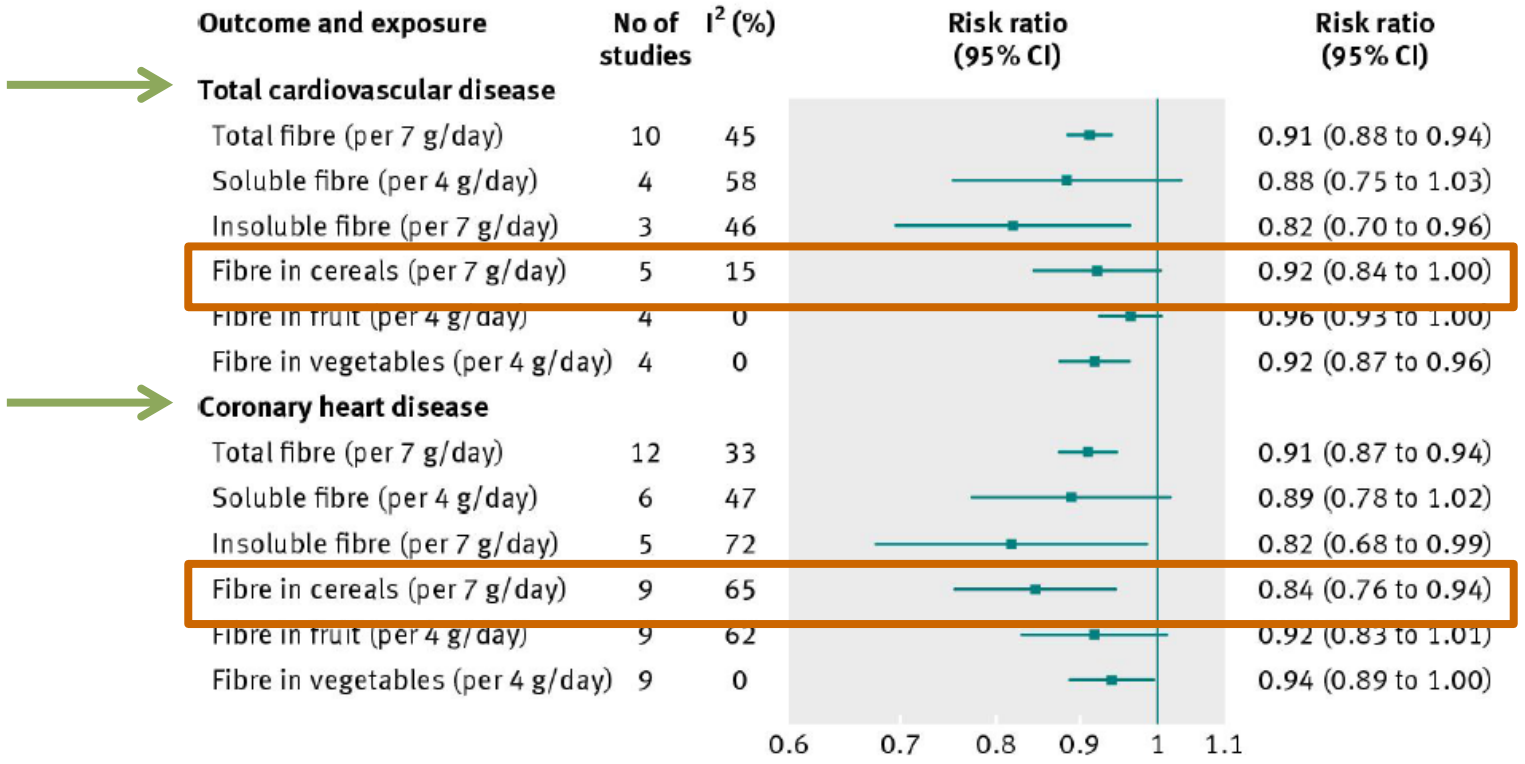
Recommended by FAO



Dietary Fibre and CVD

Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis

Diane E Threapleton *doctoral student*[1], Darren C Greenwood *senior lecturer in biostatistics*[2], Charlotte E L Evans *lecturer in nutritional epidemiology*[1], Christine L Cleghorn *research fellow*[1], Camilla Nykjaer *research assistant*[1], Charlotte Woodhead *research assistant*[1], Janet E Cade *professor of nutritional epidemiology group*[1], Christopher P Gale *associate professor of cardiovascular health sciences*[2], Victoria J Burley *senior lecturer in nutritional epidemiology*[1]

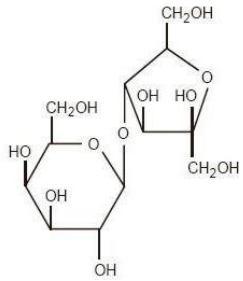


Threapleton et al. (2013) BMJ

Health Claims and Dietary Fibre evaluated by EFSA

- *Dietary fibre is not sufficiently characterized in relation to claimed effects*

- *Some specific dietary fiber components are considered to be sufficiently characterized*
  - pectin
  - lactulose(?)
  - wheat bran fibre, rye fibre, Konjac mannan (glucomannan),
  - hydroxypropyl methylcellulose (HPMC) guar gum, beta-glucan



β-Glucan – properties

90% cellotriosyl + cellotetraosyl, 10% longer sequences

G – G – G

G – G – G – G

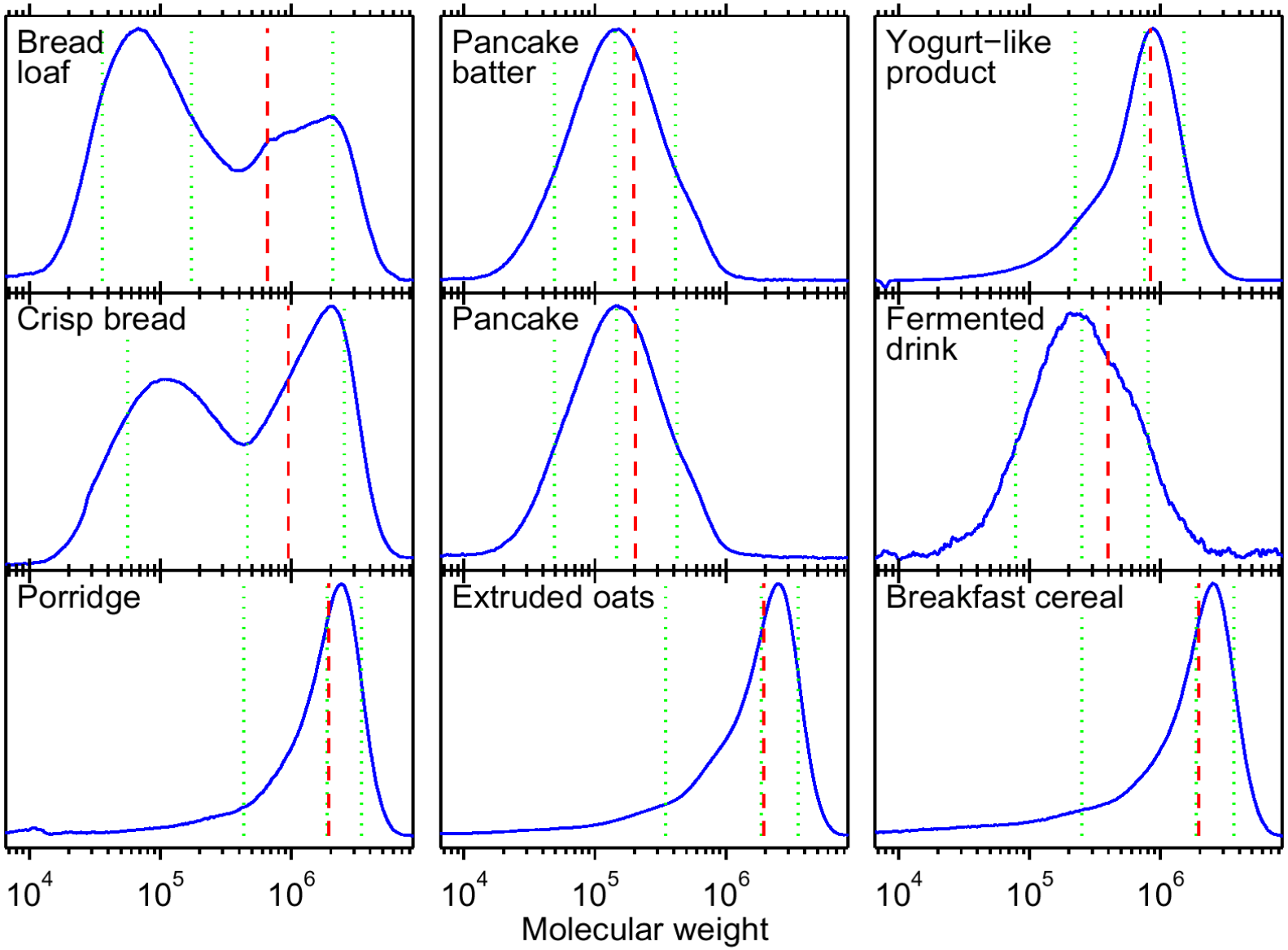
Ratio cellotriosyl/cellotetraosyl
Barley: 3.3
Oats: 2.2
Wheat: 4.5

Structure and ***molecular weight distribution*** will influence properties such as ***solubility***, **viscosity, gel formation** and ***nutritional effects***

EU authorised Health Claims on Cereal Fibre and Cholesterol levels

Material	Health claim	Conditions of use	EFSA opinion reference
β-glucans (Bg)	Maintenance of normal cholesterol levels (Article 13.1 claim)	Daily intake of 3 g required Food with ≥ 1 g of Bg per quantified portion.	2009;7(9):1254 , 2011;9(6):2207
Oat β-glucan	Oat (respectively barley) beta-glucan has been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease *Article 14.(1)(a) claim (disease reduction claim)*	Daily intake of 3 g required Foods which provide at least 1g of oat (respectively barley) per portion	Q-2008-681
Barley β-glucan			Q-2011-00798 *and* Q-2011-00799

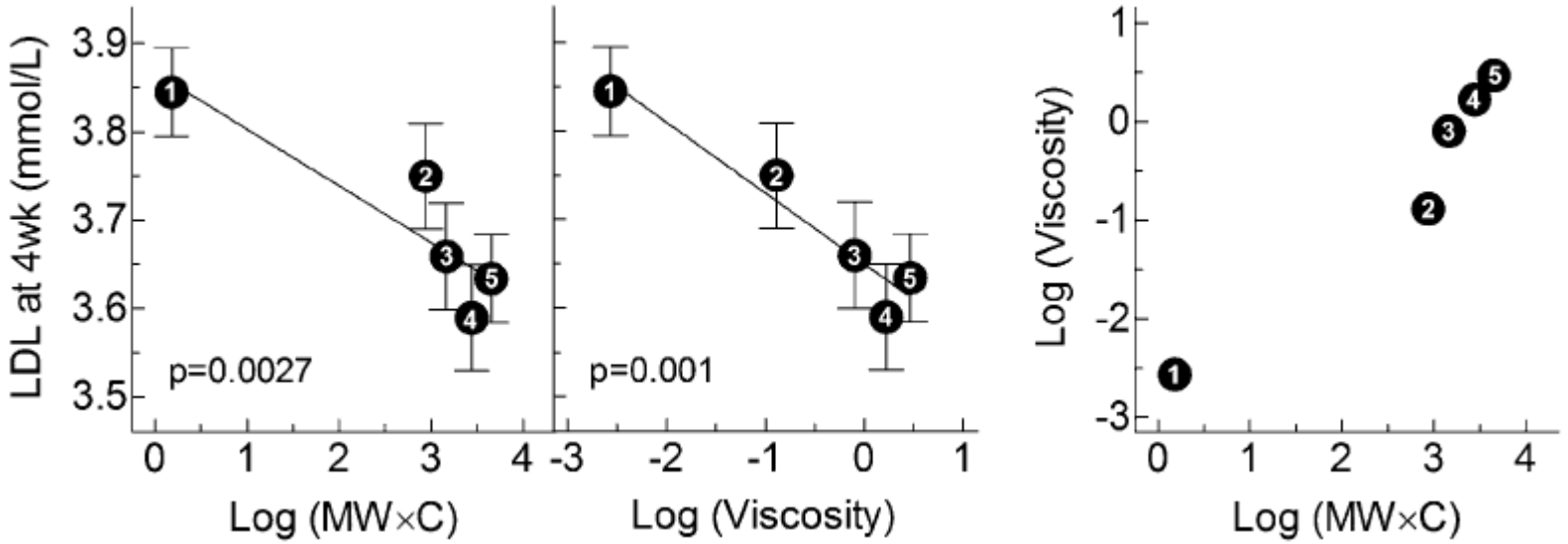
Molecular weight distributions of β-glucan in some oat foods



Effects of food processing should be considered

Physicochemical properties of oat β-glucan influence its ability to reduce serum LDL cholesterol in humans: a randomized clinical trial[1–3]

Thomas MS Wolever, Susan M Tosh, Alison L Gibbs, Jennie Brand-Miller, Alison M Duncan, Valerie Hart, Benoît Lamarche, Barbara A Thomson, Ruedi Duss, and Peter J Wood



Conclusions:

The ***physicochemical properties*** of oat beta-glucan should be considered when assessing the cholesterol-lowering ability of oat-containing products

Wolever et al. Am J Clin Nutr 2010;92:723–32

Other Health Claims on Fibre?
- *Cereal Fibre* and *Bowel Function*

Material	Health claim	Conditions of use	EFSA opinion reference
Rye fibre	Normal bowel function	Foods should be high in that fibre (i.e. fibre ≥ 6g/ 100g product) and daily intake ≥ 10g is required	2011;9(6**):**2258
Barley grain fibre	Increase in faecal bulk		2011;9(6):2249
Oat grain fibre	Increase in faecal bulk		2011;9(6):2249
Wheat bran fibre	Increase in faecal bulk		2010;8(10):1817
Wheat bran fibre	Accelerated intestinal transit	Foods should be high in that fibre and daily intake ≥ 10g is required	2010;8(10):1817

EU authorised Health Claims on Cereal Fibre and *reduced glucose rise* after a meal

Material	Health claim	Conditions of use	EFSA Opinion Reference
Arobinoxylan produced from wheat endosperm	Reduction of blood glucose rise after a meal	Daily intake ≥ 8g AX rich fibre	2011;9(6):2205
β-glucans from oats and barley		Intake ≥ 4g / 30g digestible carbs	2011;9(6):2207
Resistant starch (RS)		RS Content ≥ 14% of total starch	2011;9(4):2024

- Rather few indications on grain constituents have proven sufficient evidence to allow EFSA-health claims
- Often a discripancy between results from epidemiology and RCTs
- Firm characterization of material investigated has typically been lacking
- Difficult to attribute health effects to specific components due to confounding
- More research is needed!

Results from recent studies on the metabolic effects of added *prebiotic fibre* and *fermented rye bran*

The role of ***fermentation*** on ***appetite*** and ***metabolism***

Can the effect be enhanced by adding fermentable dietary fibre and plant protein ?

APPETITE

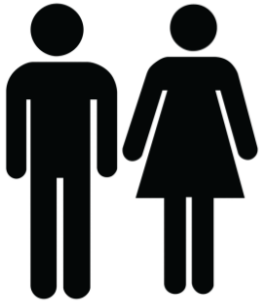
Glucose and insulin

GLP-1

Gut fermentation

I. Lee, S. Lin, DL. Webb, PM. Hellström, U. Risérus, R. Landberg (2016) *Submitted*

Participants, Measurements and Diets



21 healthy men and women
Age 38.6 ± 11.8 years
BMI 24.9 ± 3.3 kg/m^2

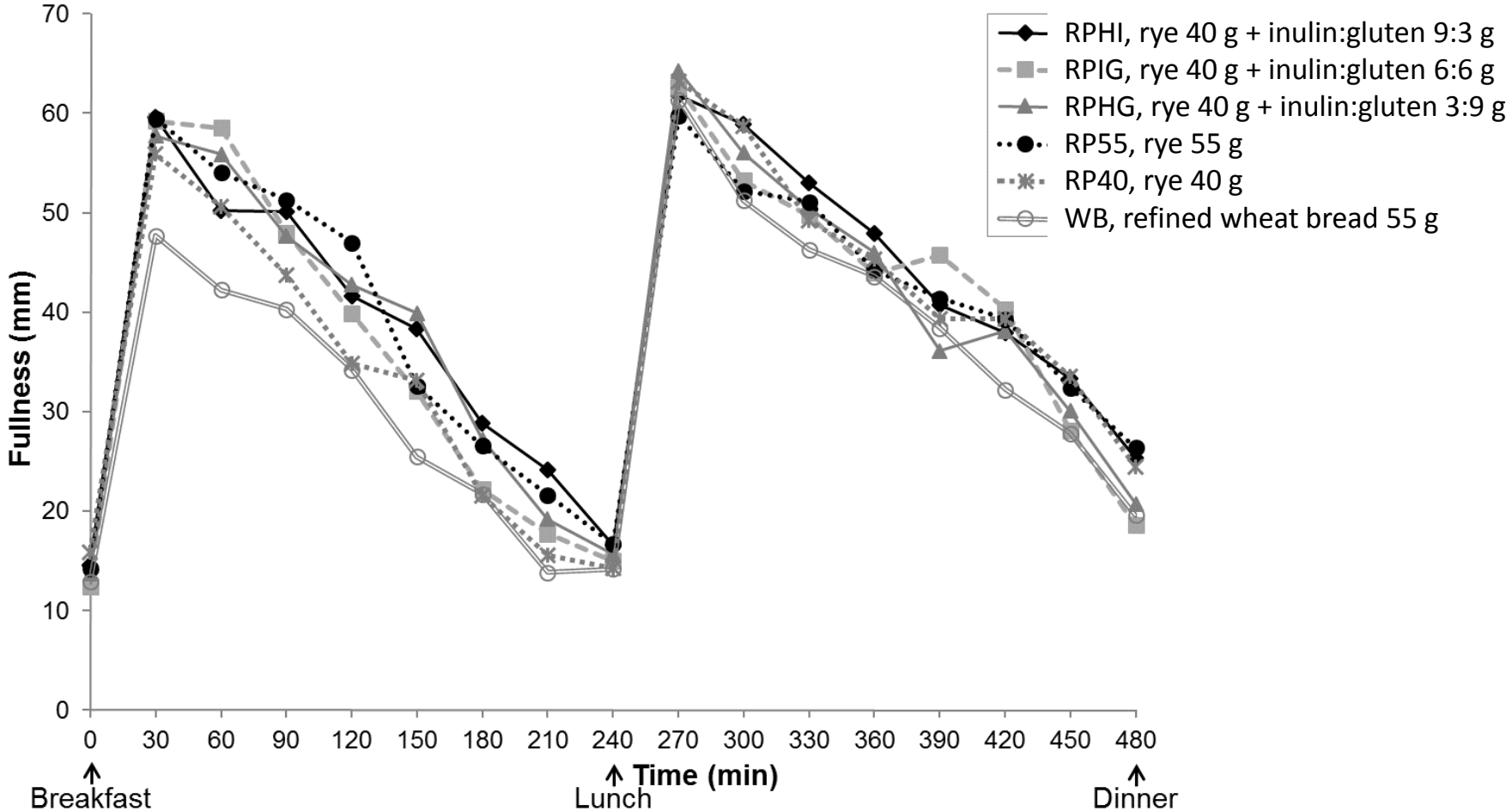
Cross-over design

- Rye porridge 40 g + 9 g inulin + 3 g gluten
- Rye porridge 40 g + 6 g inulin + 6 g gluten
- Rye porridge 40 g + 3 g inulin + 9 g gluten
- Rye porridge 40 g
- Rye porridge 55 g
- Refined wheat bread 55 g (control)

Served with raspberry jam, margarine (energy adjusting), milk, coffee/tea

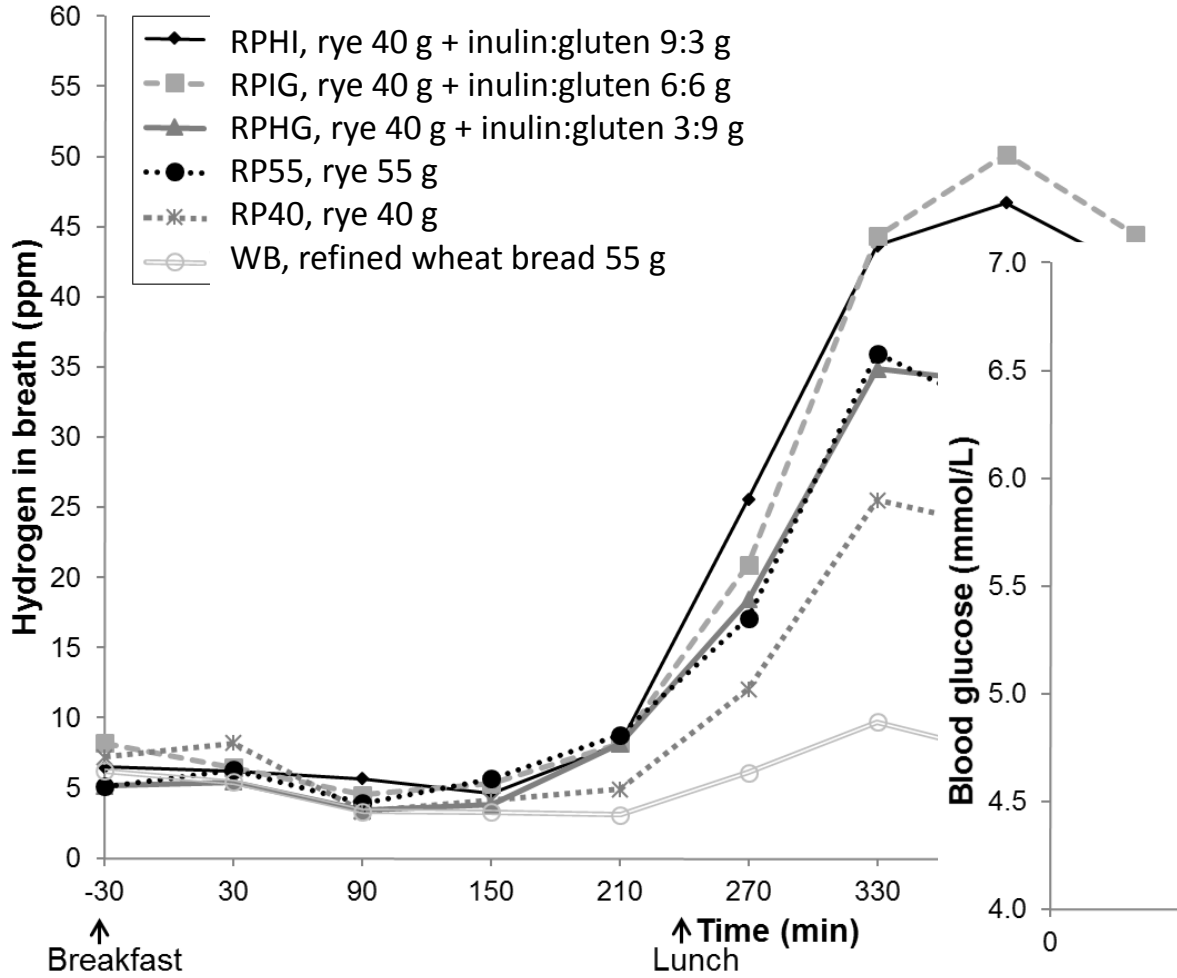
Appetite Results

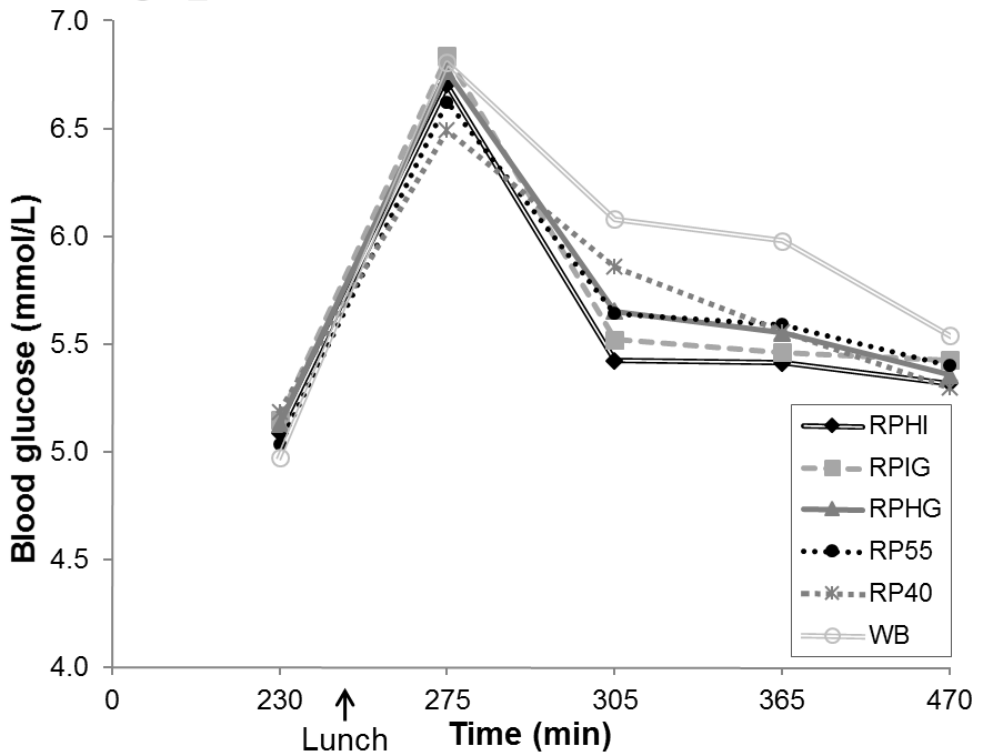
- WG rye suppressed appetite
  - Portion size dependent
- No enhanced effect of adding fibre and protein
- No differences in voluntary food intake at dinner



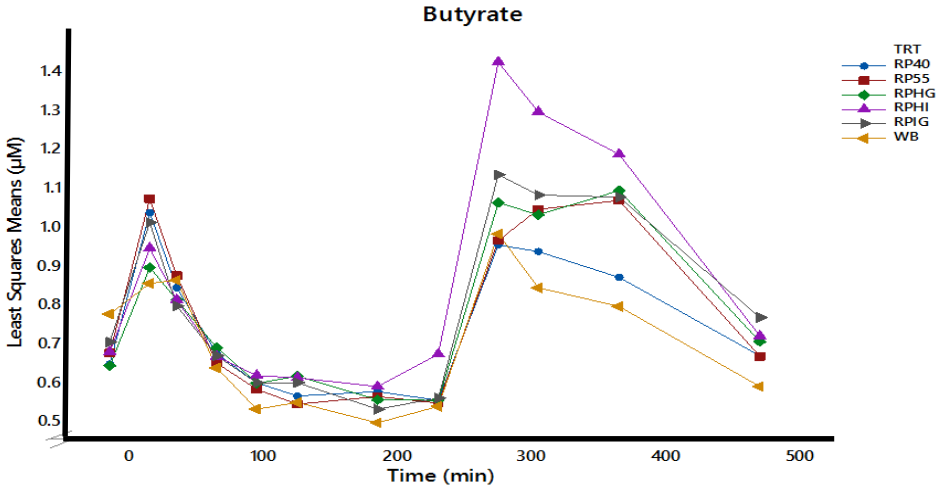
Gut fermentation & glucose results

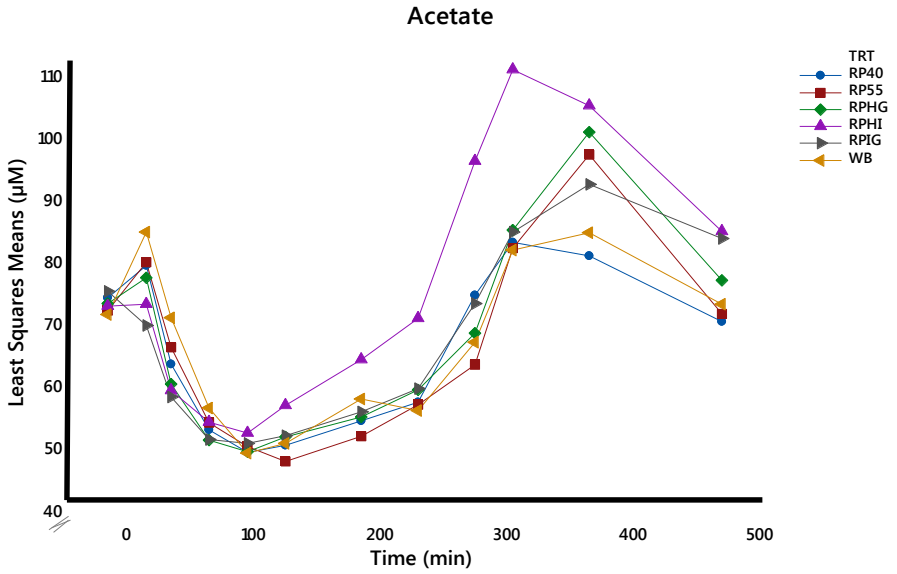
- Extensive gut fermentation
- WG rye lowered 2nd meal glucose
- No differences in insulin or GLP-1.





Short chain fatty acids in plasma





A new, rapid and sensitive GC-MS method for high-through put analysis of SCFA in different matrixes has been developed and validated

Plasma SCFA increased with increased fibre intake

No association between SCFA and plasma glucsoe second meal effect

No association with GLP-1

Lin et al (2016) Manuscript
& Wu et al (2016) Manuscript

NMR-based metabolomics to investigate extended postprandial effects of rye based porridges and refined wheat bread

- Rye porridges with added inulin and gluten
- Refined wheat bread

Glucose / Insulin / Appetite

Metabolites

☺	-15 min	8.05 am
	breakfast	8.20 am
☺	35 min	8.55 am
☺	65 min	9.25 am
☺	185 min	11.25 am
☺	230 min	12.10 am
	lunch	12.20 am
☺	305 min	13.25 pm
☺	365 min	14.25 pm
☺	470 min	16.10 pm

Bruker spectrometer (600 MHz)

Amino acids and their catabolic products

Metabolites	Buckets (ppm)	QC (cv%)
2-hydroxybutyrate	0.9025±0.0025	4.8
2-oxoisocaproate	0.9475±0.0025	5.8
Leucine	0.975±0.005	2.6
Isoleucine	1.015±0.005	4.3
Valine	1.0375±0.0025	4.2
Alanine	1.475±0.005	2.5
Lysine	1.7325±0.025	2.5
Glutamate	2.363±0.005	4.5
Glutamine	2.475±0.005	3.1
Methionine	2.655±0.005	3.6
Sarcosine	2.755±0.005	14.9
Asparagine	2.875±0.005	7.3
Creatine	3.0425±0.0025	4.2
Serine	3.965±0.005	4.3
Creatinine	4.065±0.005	4.1
Proline	4.1475±0.0025	8.5
Histidine	7.1 ±0.01	2.9
Phenylalanine	7.325±0.005	3.5

Diet effect ***Gender effect***

Diet x Time ***Gender x time***

Ketone bodies

Metabolites	Buckets (ppm)	QC (cv%)
3-hydroxybutyrate	1.205±0.005	5.5
Acetone	2.235±0.005	10.9
Acetoacetate	2.285±0.005	2.9

Glycolytic and TCA intermediates

Metabolites	Buckets (ppm)	QC (cv%)
Glucose	3.913±0.005	5.2
Lactate	1.335±0.005	4.9
Pyruvate	2.375±0.005	5.8
Succinate	2.405±0.005	8.3
Citrate	2.525±0.005	3.19

Fermentation product

Metabolites	Buckets (ppm)	QC (cv%)
Acetate	1.925±0.005	4.4

Other metabolites

Metabolites	Buckets (ppm)	QC (cv%)
Propylene glycerol	1.155±0.005	12.2
Dimethylglycine	2.925±0.005	8.2
Dimethyl sulfone	3.155±0.005	3.8
O-acethylcarnitine	3.195±0.005	2.5
Choline	3.205±0.005	2.8
Carnitine	3.225±0.005	4.3
Betaine	3.265±0.005	2.8
Myo-insitol	4.0725±0.0025	6.9
Formate	8.455±0.005	9.3

Findings

- All rye porridges 55g vs. refined wheat bread
  → reduced appetite during 8h
- *Portion size > 40g is needed to get beneficial effects*
- No difference in insulin concentrations between treatments
  Microstructural explanations?
- Gut fermentation increased with increased fibre intake
- *No relationship between second meal effect and SCFA*
- *Appears that rye, not added inulin and subsequent SCFA affected second meal glucose*
- *What is the role of gut fermentation and SCFA in appetite regulation? Other mechanisms?*

The RyeClaim-project: Effects of fermented rye products on *Helicobacter pylori* infection & metabolic risk factors

Research Consortium

VINNOVA

FUDAN UNIVERSITY 1905

Lantmännen

wasa Barilla The Italian Food Company. Since 1877.

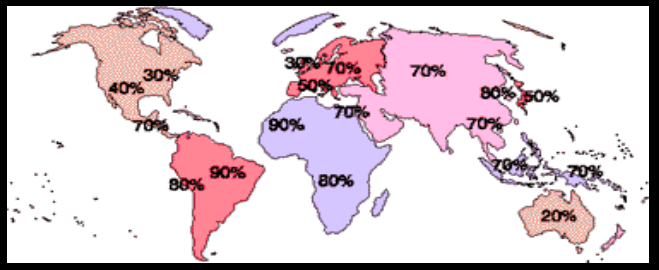
UMEÅ UNIVERSITET

SLU

AIM: To develop innovative rye-based food products for prevention and relieve of H. pylori infections, chronic inflammation and T2D risk factors

Duration: 2014-2016

Helicobacter pylori – bacterium of peptic ulcer



- *About 50% of the world population is infected by Helicobacter pylori*
- *H. pylori infection leads to gastritis (inflammation in the stomach)* 20% of HP infected individuals will develop peptic ulcer
- HP infection increases the risk of developing gastric cancer
- Traditional therapy: Proton pump inhibitors (such as Losec®) + two different antibiotics during 7 days
- Alternative methods to relive symptoms and prevent HP adhesion (colonisation) in the stomach are needed

Promesing results on bacterial load and adhesion:
Combination of rye bran + *specific LAB*

A large long-term study needed to proof concept!

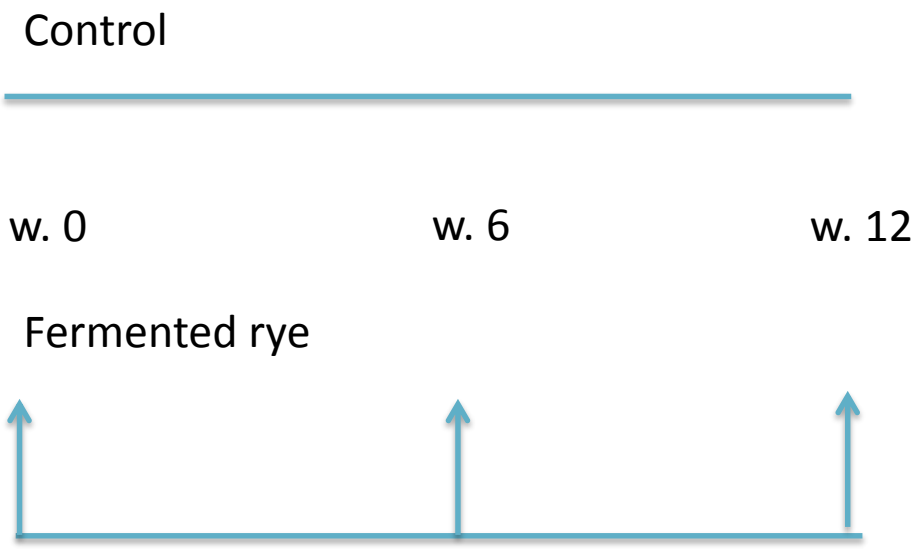
Study design

- Randomized controlled parallel single blinded 12 wk intervention
- Refined wheat or WG rye with added fermented rye bran
- Products provided about 20% daily energy intake and 30 g dietary fibre
- Body weight and body fat secondary outcomes

Screening (n=569 subjects)

- Helicobacter pylori positive
- Overweight/obese or normal weight (50%:50%)
- No antibiotics treatment
- Men and women
- Randomize 180 subjects

1-2 months

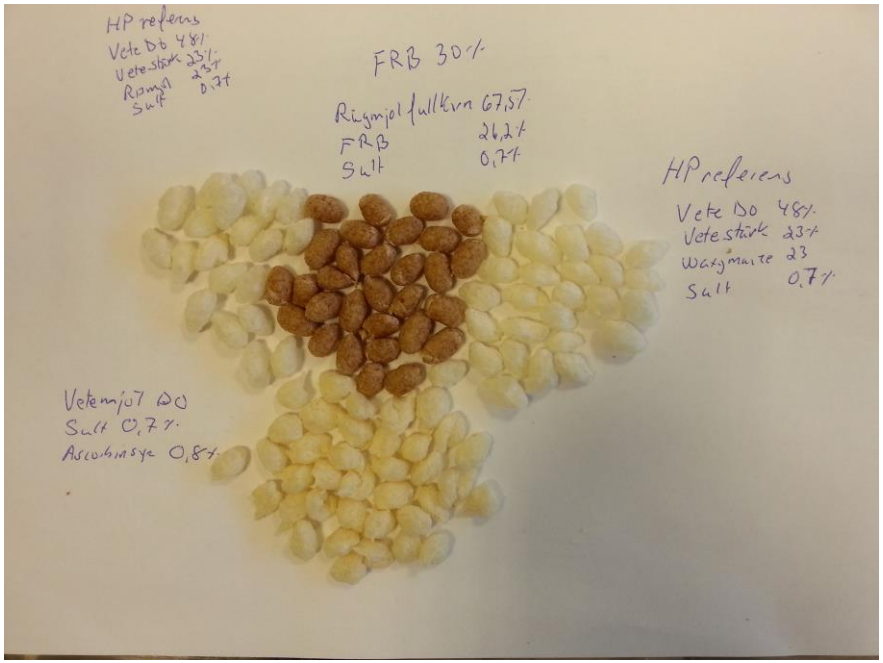


w. 0	w. 6	w. 12
Breath test	Breath test	Breath test
Blood samples	Blood samples	Blood samples
Weight & body fat	Weight & body fat	Weight & body fat
Fecal sample	Fecal sample	Fecal sample

Test products

Active products contained 25% fermented rye bran and control products were made of refined wheat.

[redacted]



Daily product intake

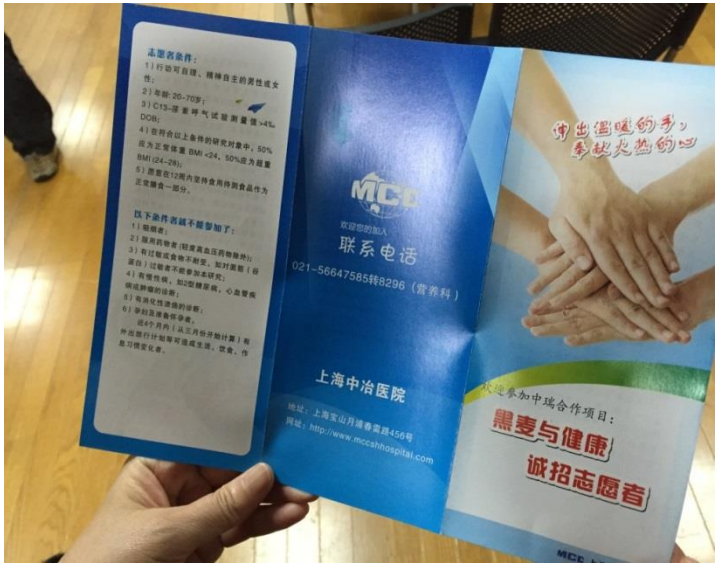
4 slices of crisp bread and **84/110** grams of puffs

Product	Amount (g)	Energy (kcal)	Dietary fiber	Protein	Fat	CHO	Water	Ash
Fermented rye bran (FRB)								
FRB crisp	44.8	145.5	11.1	4.3	1.2	23.9	3.2	1.2
FRB puff	110	371.6	26.3	11.4	3.3	61.2	5.0	2.8
SUM FRB	**154.8**	**518.1**	***37.4***	**15.7**	**4.5**	**85.1**	**8.2**	**4.0**
Refined wheat (RW)								
Wheat crisp	**58.8**	**210.5**	**3.6**	**6.8**	**1.0**	**41.2**	**4.5**	**1.1**
Wheat puff	**84**	**302.7**	**8.6**	**9.7**	**1.6**	**58.1**	**4.9**	**1.4**
SUM RW	**142.8**	**513.2**	**12.2**	**16.4**	**2.6**	**99.3**	**9.4**	**2.3**

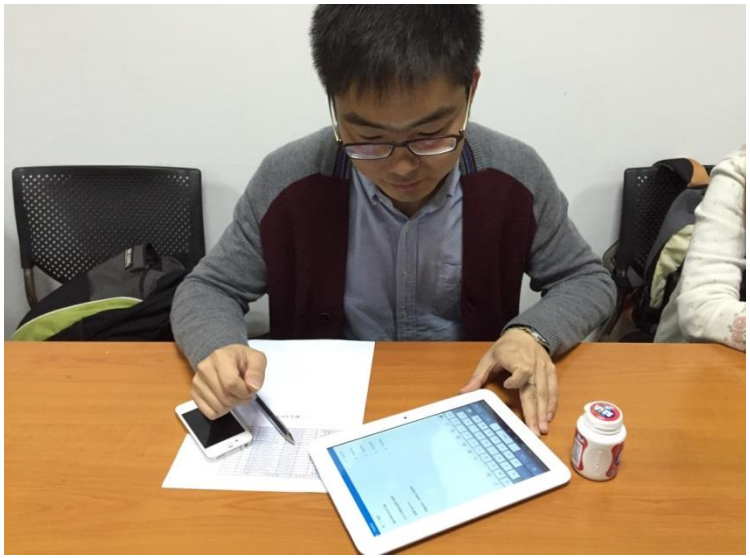
Execution of the study

Staff involved for collection of base-line data at the health care center.

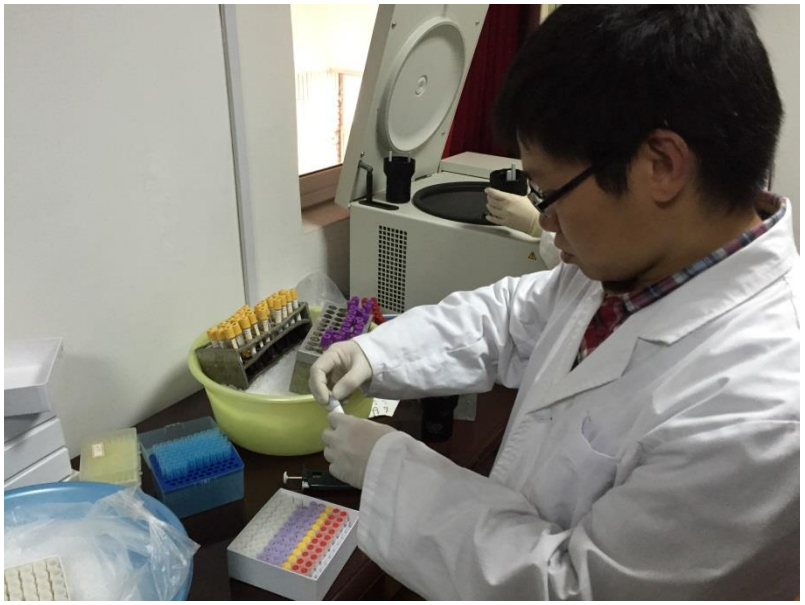
Study centre

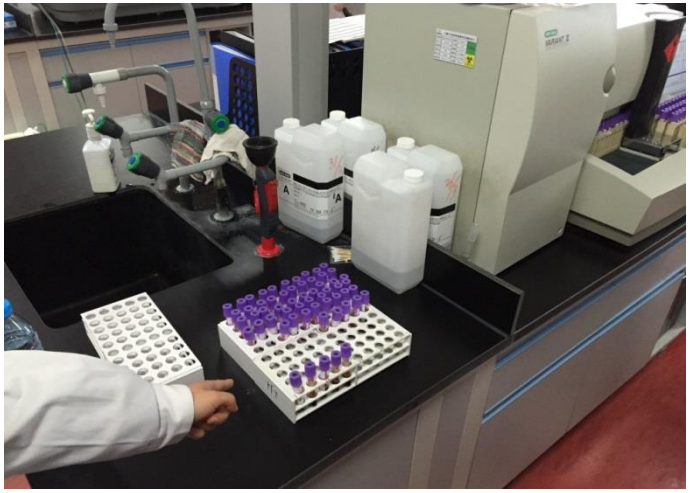


Sampling



Handling of samples





RESULTS

Screening
n=569

HP test
n=558

Exclusion
N=54
(age>70,smokers, taking antibiotic or other medicine)

HP test +
N=316(56.6%)

Inclusion
n=262人

Subjects
N=180

VAS test
N=60

FRB
N=90

n=2
1 out from SH
1 fell ill and need to take medication

FRB(BL)
N=88

n=5
1 with severe diarrhea
1 out from SH
3 can't to eat

FRB(6W)
N=83

n=3
1 with waist sprains(just left the blood sample)
1 unwilling to eat
1 catched a severe cold and took biotic

FRB (12W)
N=80

FRB(24 W)
N=64

WB
N=90

n=3
2 out from SH
1 unable to present on the visiting day due to work

WB(BL)
N=87

n=3
1 out from SH
1 moved to another workplace
1 can't to eat

WB(6W)
N=84

n=3
1 with severe diarrhea
,
1 out from SH，
1 with waist sprains
1 non-fasting

WB (12W)
N=80

WB (24 W)
N=60

Results- so far…

- No significant effect in primary outcome measurement
- 4% lower total cholesterol after 12 wk on fermented rye bran vs refined wheat
- 6% lower LDL after 12 wk on fermented rye bran vs refined wheat
- Secondary analysis to be conducted including data on compliance
- Appetite and food liking data to be analyzed

The role of cereal constituents and ingredients for health- conclusions

- Beneficial physiological effects have been proven for specific dietary fibre
- Evidence for bioactive compounds are inconclusive
- More emphasis should be put on the role of processing
- More long-term randomized controlled trials are needed with well characterized material
- OMICS-technologies should be in more extensivly incorporated in RCTs and observational studies to better understand the mechanisms

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