To fiber or not to fiber

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Soeterbeeck
2024

Disclosure of Conflicts of Interest:

- Personal fee from invited speaker by Janssen
- Personal fee from invited speaker Cedar Sinai Medical Center

Voedingsvezel

- Niet verteerbare complexe koolhydraten in planten
- gegroepeerd naar hun (on)oplosbaarheid in water
- Mensen missen vezelspecifieke enzymen om deze vezels te verteren

Andersen V, et al. J. Crohns Colitis. 2018;12:129–136. doi: 10.1093/ecco-jcc/jjx136.

Definitie van voedingsvezel

Voedingsvezels bestaan uit koolwaterstof polymeren met ≥3 monomere eenheden(MU), die noch verteerd noch geabsorbeerd worden in het menselijk MDK en omvatten:

- Non-starch polysaccharides (NSP) (MU≥10)
  - cellulose, hemicellulose, pectins, hydrocolloids (i.e. gums, mucilages, ß-glucans)
- Resistant starch (MU≥10)
- Resistant (non-digestible) oligosaccharides (ROS) (MU 3-9)
  - (e.g. fructo-oligosaccharides: FOS, galacto-oligosaccharides: GOS)

Discussie over inclusie van lignine and ROS

WHO/FAO (2009) Report of the 30th session of the Codex Committee on Nutrition and Foods for special dietary Uses, no ALINORM 02/32/26.

Geschiedenis van voedingsvezel inname

Jagers/verzamelaars

landbouw

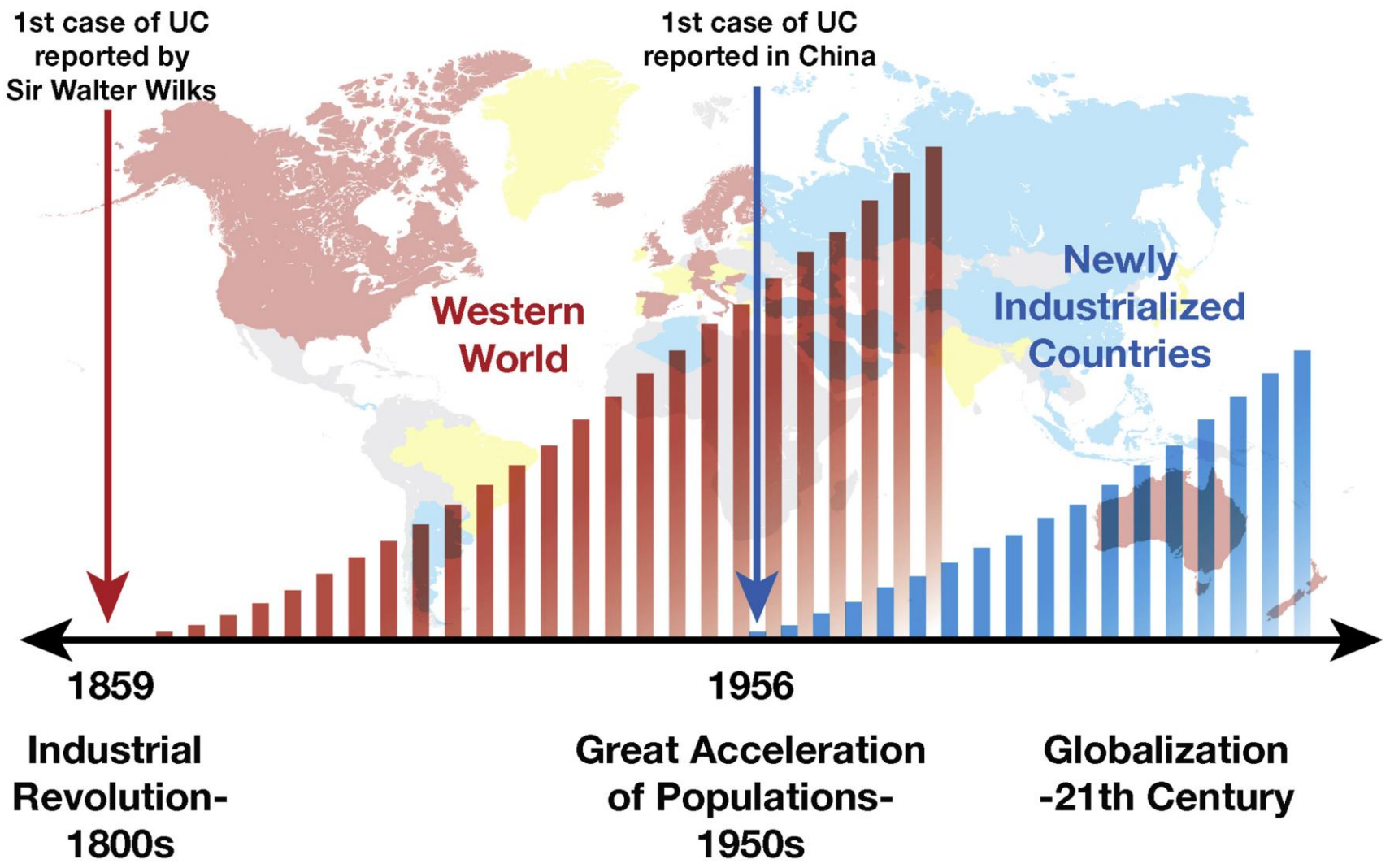
processed food

200 150 100 50 10 x1000 jaar

100-150g

35g

15g vezel inname/dag



Kaplan Understanding and Preventing the Global Increase of Inflammatory Bowel DiseaseGastroenterology. 2017 Feb;152(2):313-321

Aanbevolen hoeveelheden

In Europa a total fibre intake of 3-4 g/MJ per day:

- 25-32 g/d volwassen vrouwen
- 30-35 g/d volwassen mannen

Actueel gemiddelde inname in Westerse landen:

- 16-20 g/d volwassen vrouwen
- 18-24 g/d volwassen mannen (↑H, N and SF and ↓CA and US)

Geen aanbevelingen voor specifieke vezels

Stephen AM, et al. *Nutrition Research Reviews* (2017), **30**, 149-190

Huidige vezelinname

- Graan producten 32-49%[1] (IRL, NL, S↑)
  - Brood: 11-30%
  - Ontbijtgranen: 3-11%
  - Pasta: 1-4%
- Groente, aardappelen en fruit[1]
  - Groente:12-21%
  - Aardappelen: 6-19% (Noord Europa ↑)
  - Fruit: 8-23% (Zuid Europa ↑)
- Peulvruchten, knollen[2]

1. Stephen AM, et al. *Nutrition Research Reviews* (2017), **30**, 149-190
2. Andersen V, et al. J. Crohns Colitis. 2018;12:129–136. doi: 10.1093/ecco-jcc/jjx136

Laag vezeldieet in IBD

Laag vezeldieet geadviseerd bij stenose

Laag vezeldieet wordt soms geadviseerd bij mensen met **actieve** ziekte[1]

Minder voedingsvezel wordt ook vaak geadviseerd bij **inactieve** ziekte, gedeeltelijk vanwege individuele (in)toleranties[2,3].

1. Charlebois A., et al. Crit. Rev. Food Sci. Nutr. 2015;8:1370–1378. doi: 10.1080/10408398.2012.760515.
2. Triggs C.M., et al. Mutat. Res. 2010;690:123–138. doi: 10.1016/j.mrfmmm.2010.01.020.
3. Marlow G., et al.Ferguson L.R. J. Nutrigenet. Nutrigenom. 2015;8:70–80. doi: 10.1159/000435783.

Semi-vegetarisch dieet en IBD

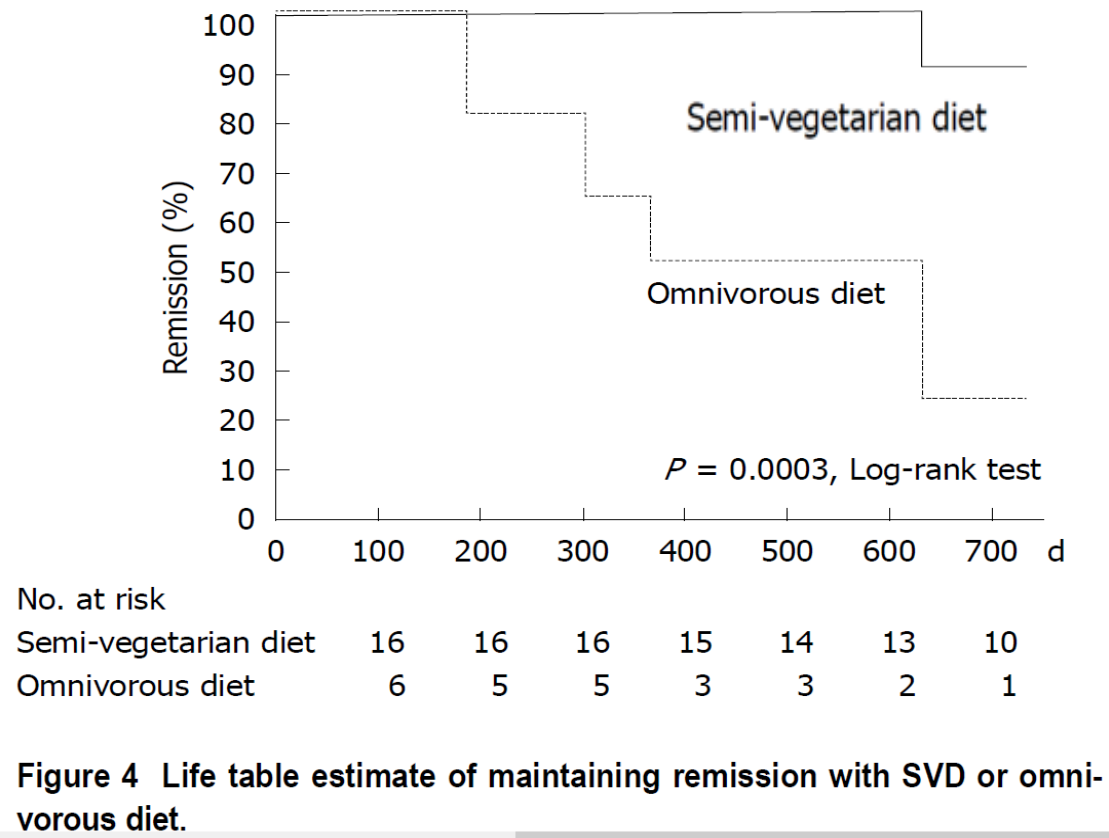


Figure 4 Life table estimate of maintaining remission with SVD or omnivorous diet.

- Een semi-vegetarisch dieet was effectief in het voorkomen van een opvlamming bij ZvC
- Geen informatie over het microbioom

Chiba M World J Gastroenterol 2010 May; 16(20):2484-2495

Vegetariërs en IBD en microbioom

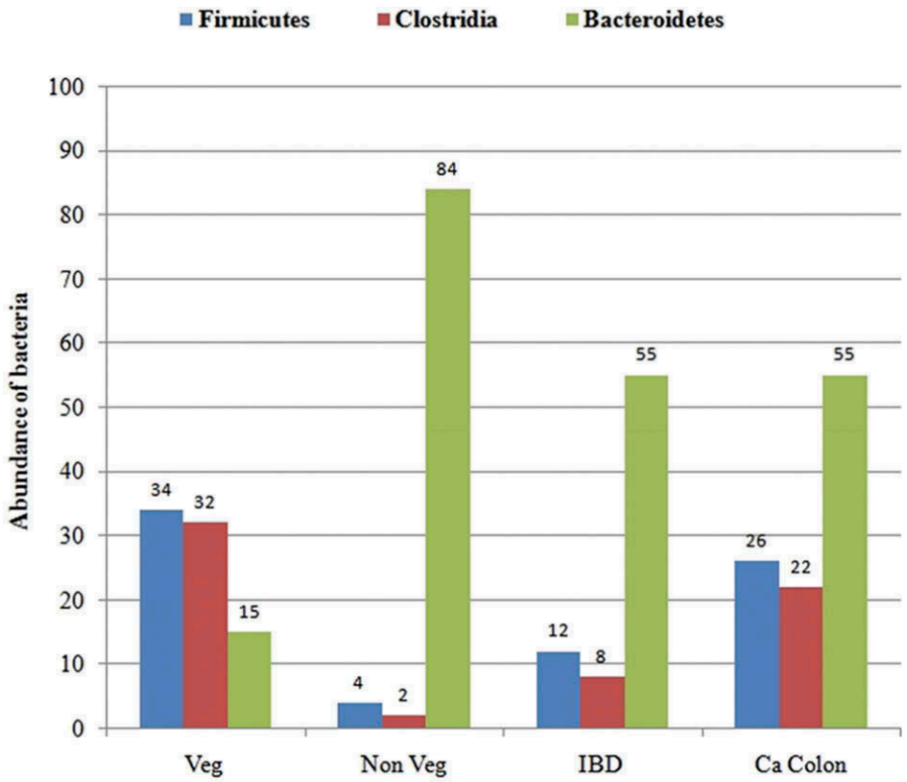


Figure 2. Abundance of major phyla in healthy subjects (Veg, vegetarian; Non Veg, non-vegetarian), a patient with inflammatory bowel disease (IBD), and a patient with colon cancer (Ca Colon).

Bamola VD Microb Ecol Health Dis 2017 May 19;28(1):1322447

Vegetariërs en IBD en microbioom

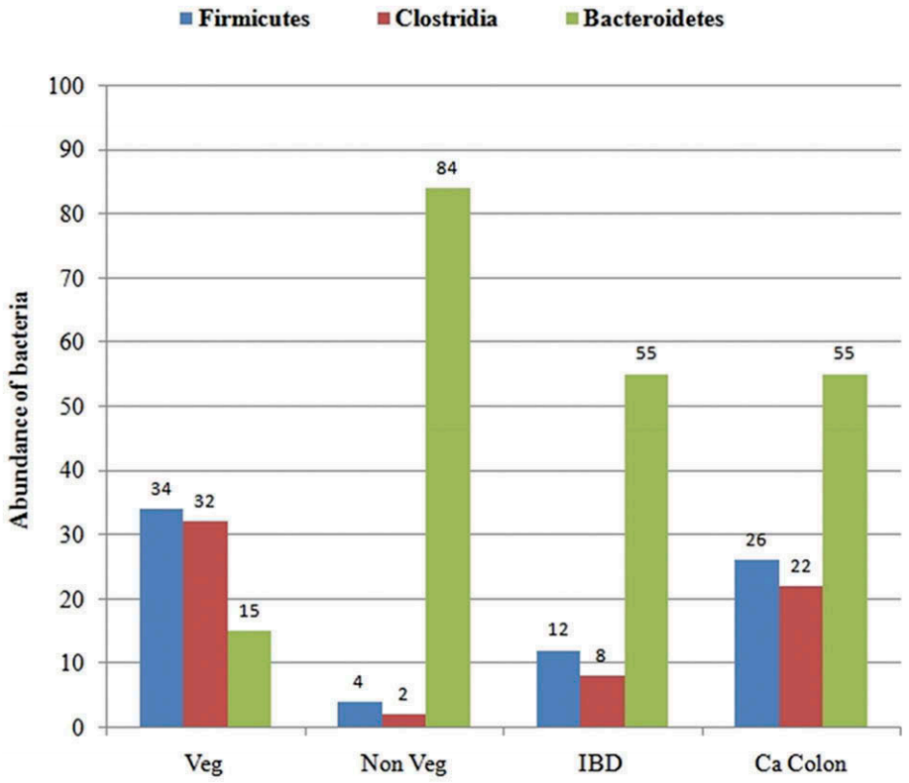
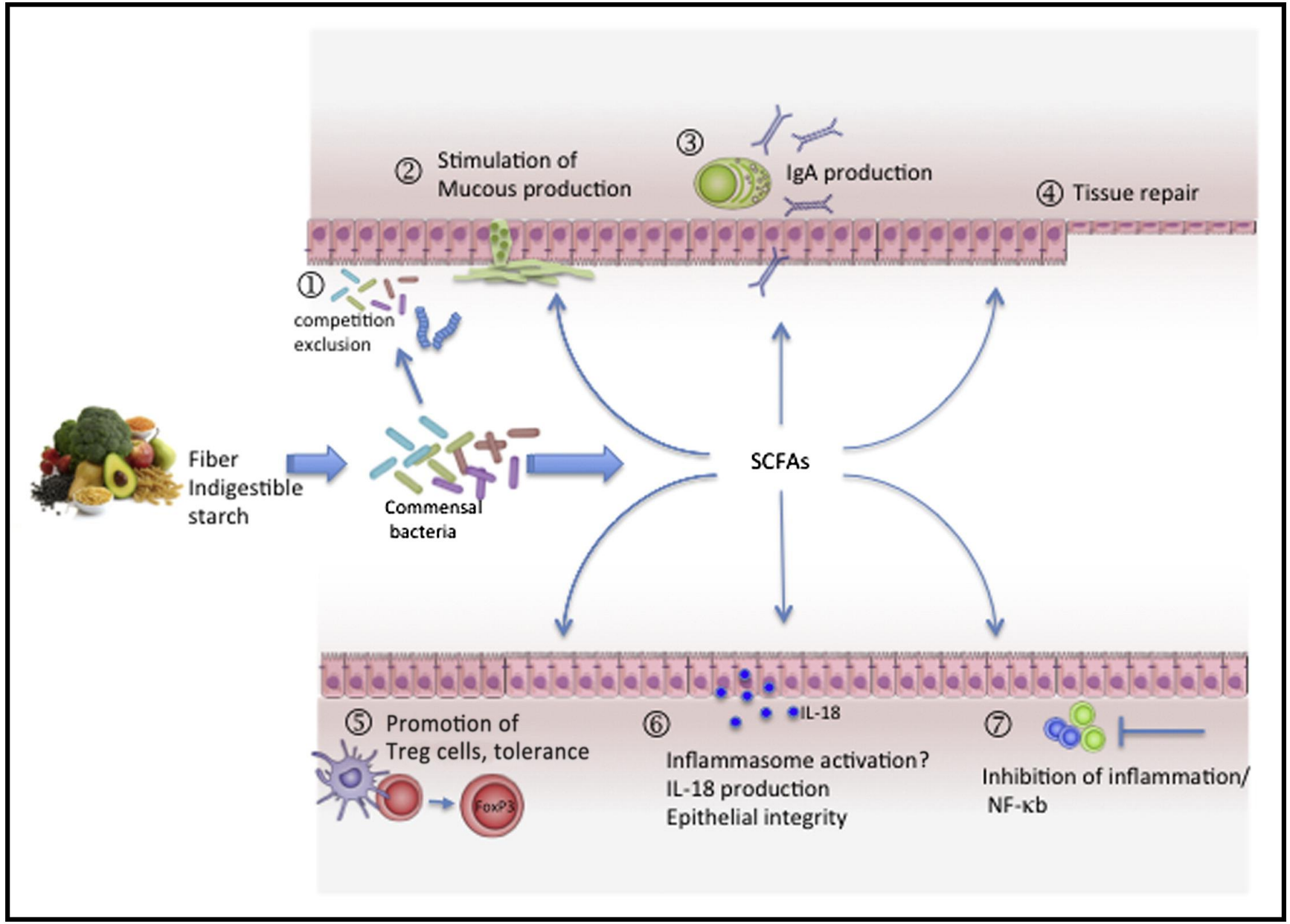


Figure 2. Abundance of major phyla in healthy subjects (Veg, vegetarian; Non Veg, non-vegetarian), a patient with inflammatory bowel disease (IBD), and a patient with colon cancer (Ca Colon).

Yao CK,. Modulation of colonic hydrogen sulfide production by diet and mesalazine utilizing a novel gas-profiling technology. Gut Microbes. 2018 Nov 2;9(6):510-522. doi: 10.1080/19490976.2018.1451280. Epub 2018 May 9. PMID: 29561196; PMCID: PMC6287689.

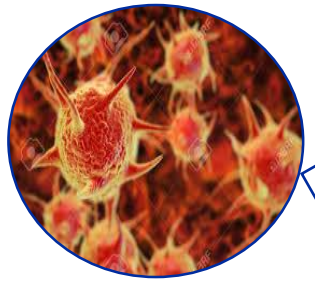


Immunity 2014 40, 833-842DOI: (10.1016/j.immuni.2014.05.014)

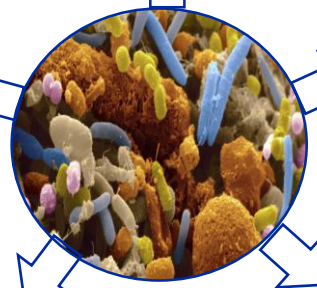
Rol van de darmbacteriën

Afbreken voedingsstoffen

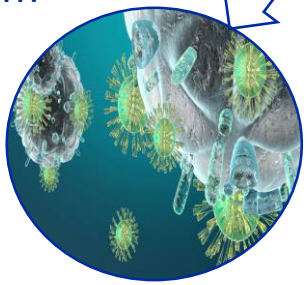
Afweren pathogene microben



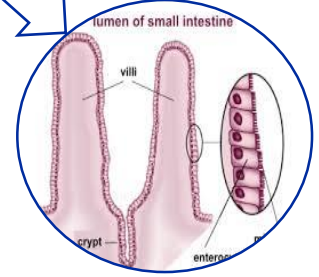
Productie vitamines



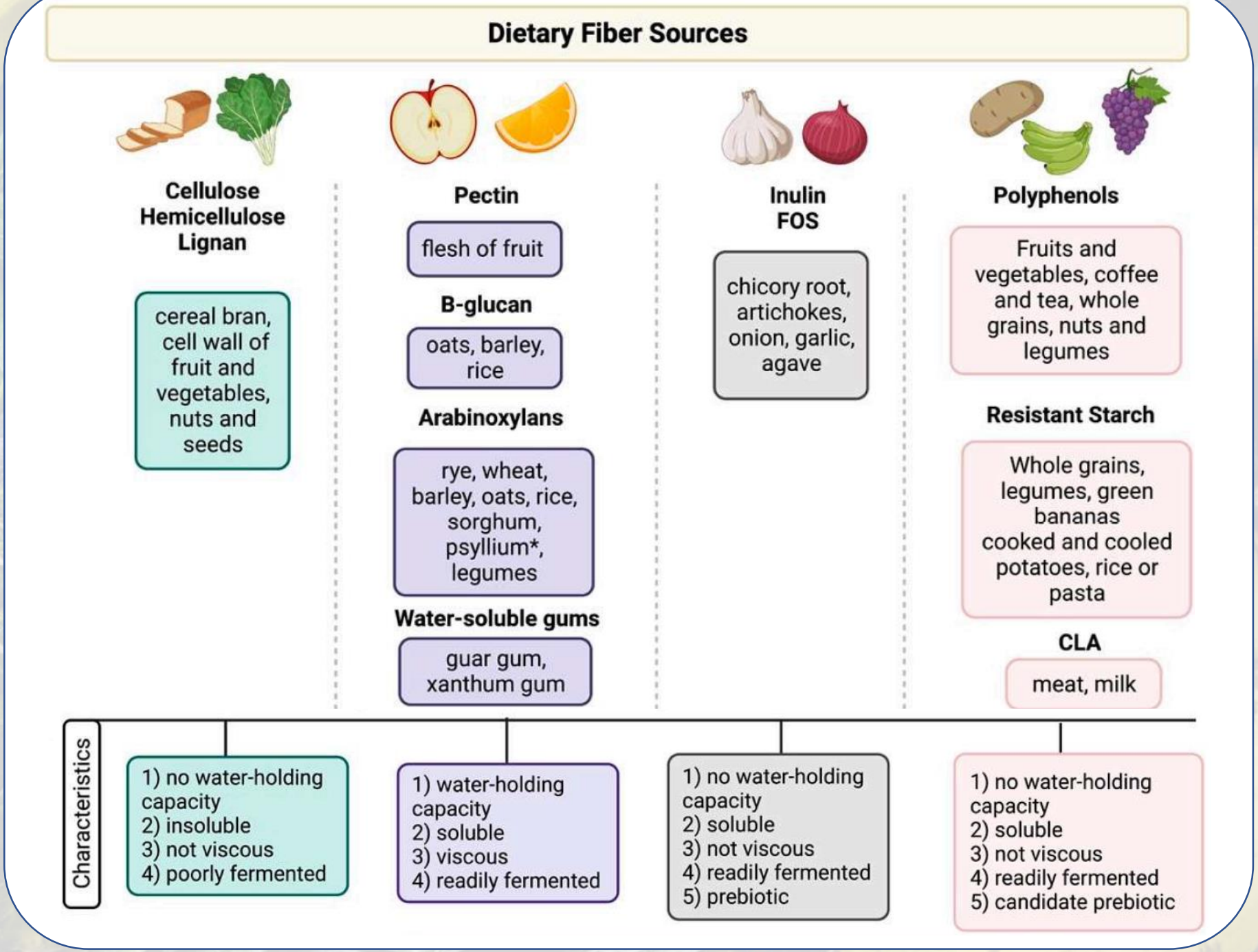
Stimuleren immuun system



Beschermen darm epitheelcellen



Soort voedingsvezel, gebaseerd op fysische eigenschappen



Bron: Haskey N, et al To Fiber or Not to Fiber: The Swinging Pendulum of Fiber Supplementation in Patients with Inflammatory Bowel Disease. Nutrients. 2023 Feb 21;15(5):1080. doi: 10.3390/nu15051080. PMID: 36904081;

Fibre evolving classifications

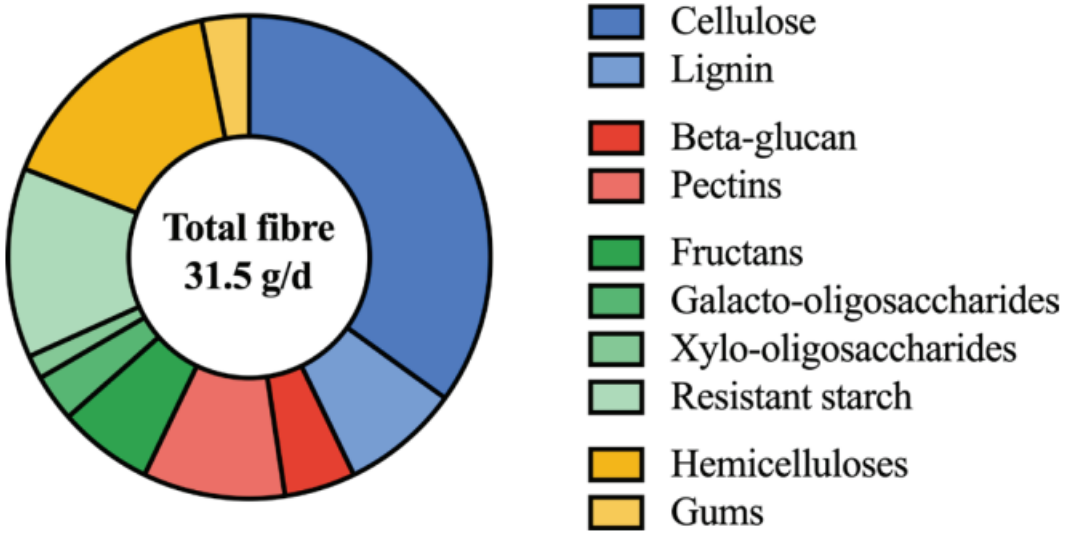


Figure 2 Percentage contribution of fibre types to average total fibre intake in a European diet, using data derived from the European Prospective Investigation into Cancer and Nutrition.[94]

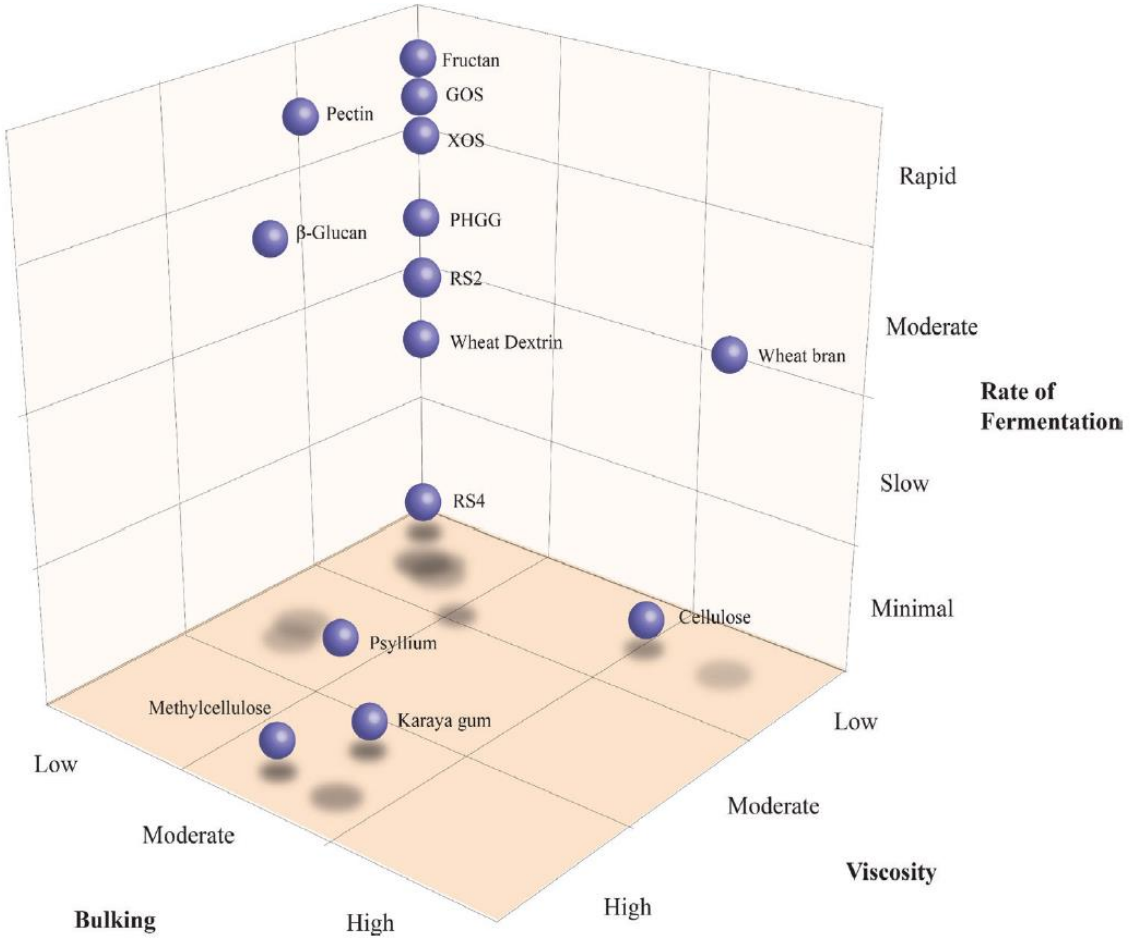


Figure 3 Overview of pure dietary fibre types (and wheat bran) and their overlapping functional characteristics. Some such as xylo-oligosaccharides(XOS), wheat bran, resistant starches (RS) have variable rates of fermentation and/or have subcomponents with different fermentability. GOS, galacto-oligosaccharides;PHGG, partially hydrolysed guar gum.

So D, et al. Gut 2021;70:2383–2394. doi:10.1136/gutjnl-2021-324891

Fibre evolving classifications

So D, et al. Gut 2021;70:2383–2394. doi:10.1136/gutjnl-2021-324891

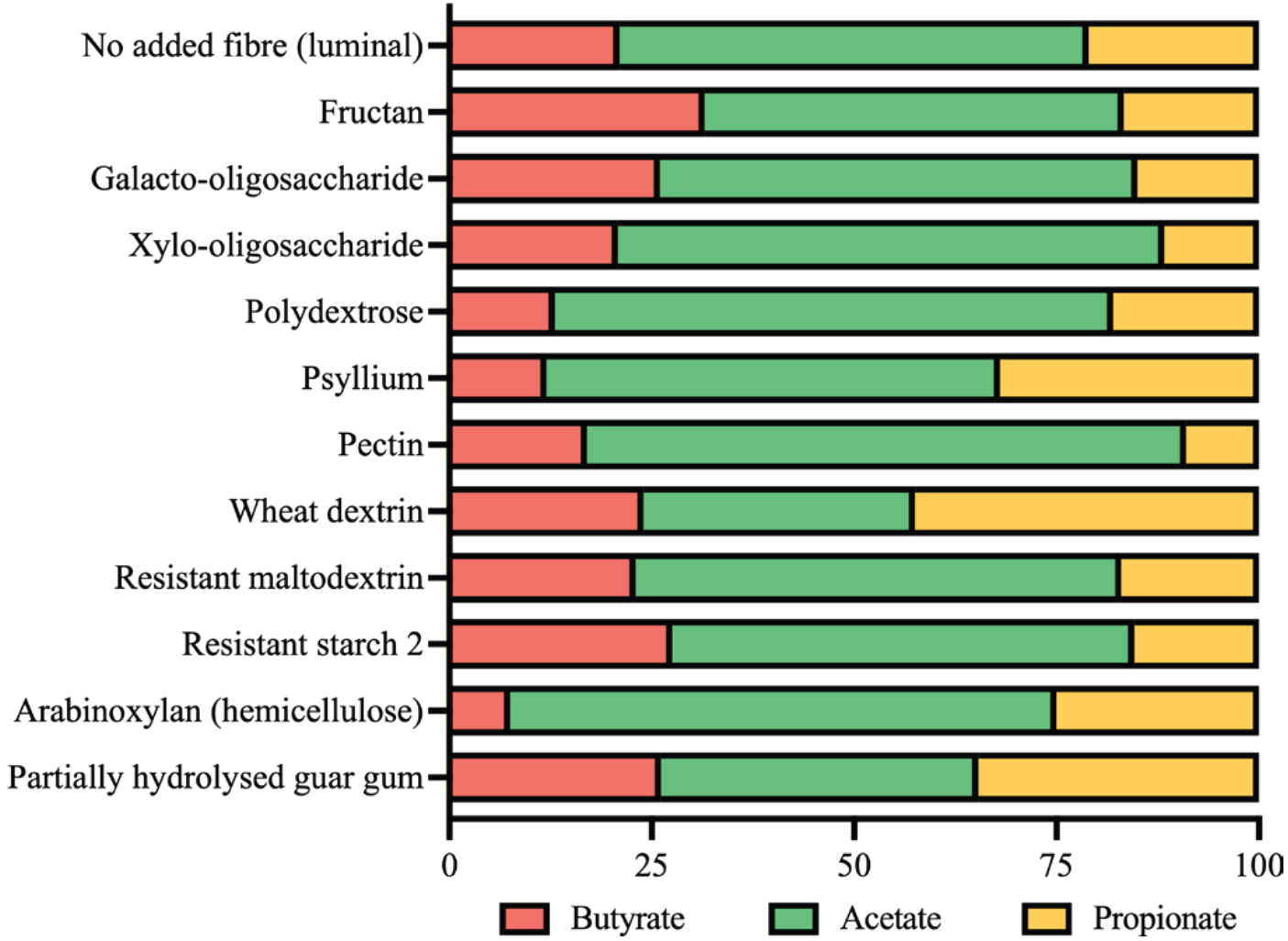
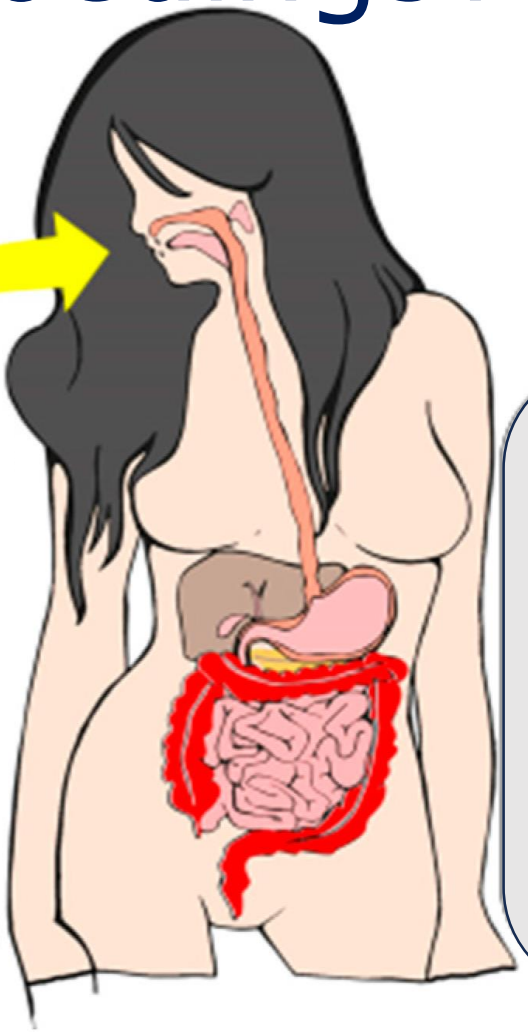


Figure 4 Metabolic profiles generated through fermentation of different fibre types in vitro using data from Alexander *et al*35 and So *et al*.34 Luminal profiles derived from Cummings *et al.*95

Functie van voedingsvezels

Inname voedingsvezel



Voordelen:
↓ maag darm passage
↑ vorm ontlasting
↓ diarrhee (oplosbaar)
↓ verstopping (onoplosbaar)

Effect op het microbioom
- Verandert samenstelling microbioom
- Productie korte keten vetzuren
- Regelt darm beweging/passage
- Zorgt voor immuun evenwicht

↓ontsteking
↑doorlaatbaarheid
↑herstel van darmwand

Wong C, et al. Int J Mol Sci. 2016 Jun; 17(6): 919. Published online 2016 Jun 14. doi: 10.3390/ijms17060919

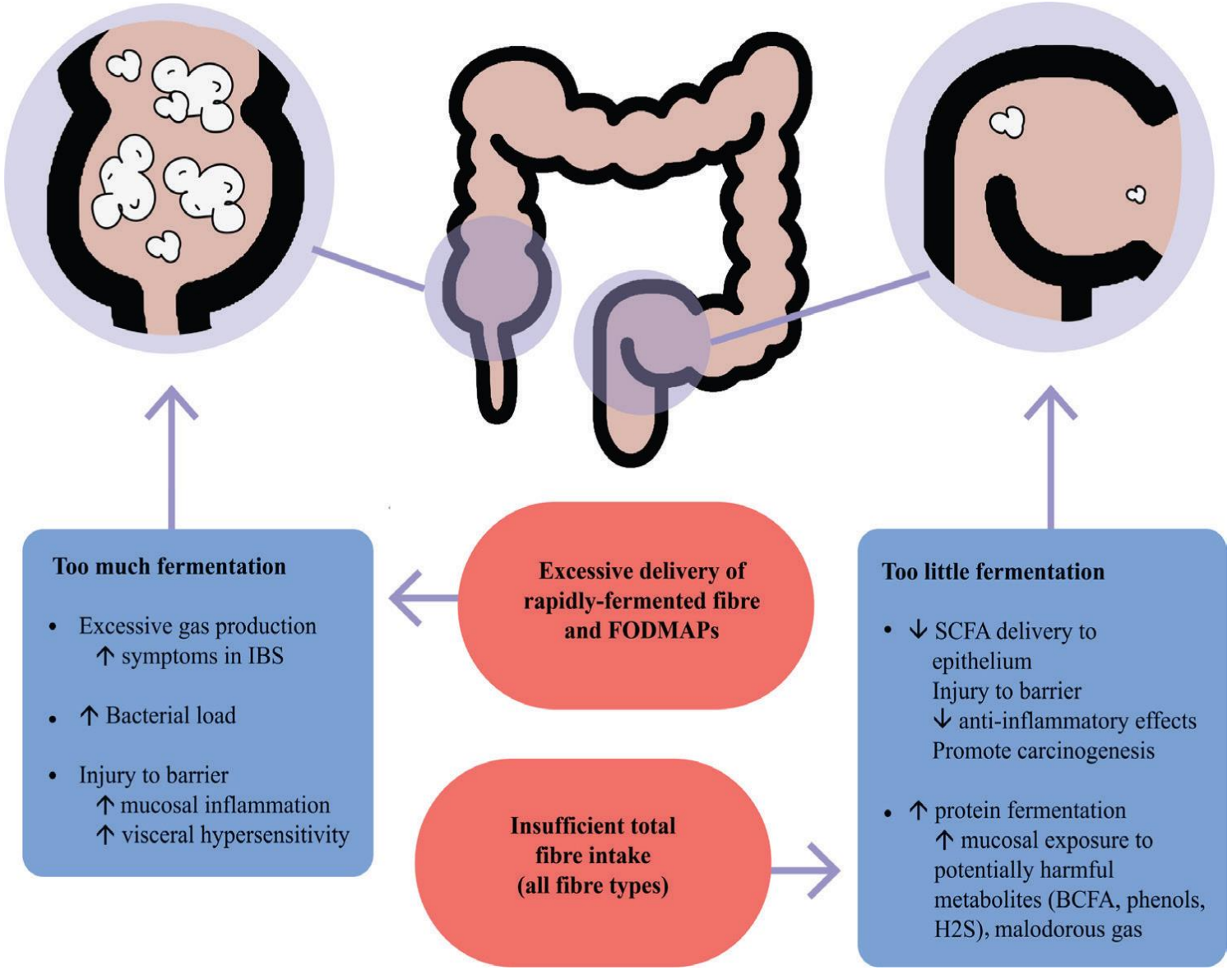


Figure 5 Adverse gut health outcomes may be precipitated through fermentation of carbohydrates (principally fibre) in the colon, including (A) excessive fermentation in the proximal colon and (B) a lack of fermentation in the distal colon. Examples of dietary intakes associated with such effects are shown in the red bubbles. BCFA, branched-chain fatty acid; FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; H2S, hydrogen sulphide; SCFA, short-chain fatty acid.

So D, et al. Gut 2021;70:2383–2394. doi:10.1136/gutjnl-2021-324891

Dietary fibre in principal food categories

Food Categories	Total dietary fibre (median g/100g)	Soluble fibre (%)	Non-starch Polysaccharides (NSP)				Resistant starch	Resistant oligo-saccharides
			Cellulose	Pectins	Hemi-cellulose	B-glucans		
Vegetables	2.2	37	+	+	++	-	-	-
Fruit								
Fresh	2.3	43	+	++	+	-	-(Except Banana)	-
Processed	1.3		+	++	+	-	-	-
Dried	5.8	53	+	++	+	-	-	-
Juice	0.4	90	+	+++	-	-	-	-
Nuts and seeds	4.2	32	+	+	++	-	-	-
Legumes	4.5	25	+	-	++	-	++	++
Potatoes, tubers	2.25	48	+	+	+	-	+	-
Leavened breads:								
White flour	3.2	50	+	-	++	-		-
Whole flour	6.4	20	+	-	++	+		+
Breakfast cereals, bars	3.4	27	+	-	++	+		+
Rice								
White	0.82	0	+	+	+		+	
Whole	3.4	13	++	+	++		+	

Simplified from: Stephen AM, et al. *Nutrition Research Reviews* (2017), **30**, 149-190

Resistant starch (RS)

RS1
Physically inaccessible starch
Whole or partially milled grains, seeds and legumes

RS2
Granular starches
Green bananas, uncooked potatoes
high amylose starches (maize)

RS3
Gelatinised and retrograded starches, enzyme-branched starches
Cooked and cooled rice, pasta and potatoes

RS4
Chemically modified
Added to bakery product

Stephen AM, et al. *Nutrition Research Reviews* (2017), **30**, 149-190
Ferguson LR, et al. In: Knasmüller S, et al. editors. Wiley-VCH Verlag; Weinheim, Germany: 2009. 721–729.

SOURCES OF
RESISTANT STARCH

(PER 100 GRAMS OR 1/2 CUP)

BEANS	BROWN RICE	GREEN BANANAS	LENTILS
2–4g	3.5g	4.7g	3.4g

MUESLI CEREAL	OATS	POTATOES
3.2g	3.6g	3.6g

Meta-Analysis > BMC Gastroenterol. 2020 Nov 10;20(1):372. doi: 10.1186/s12876-020-01516-4.

The effects of resistant starches on inflammatory bowel disease in preclinical and clinical settings: a systematic review and meta-analysis

Joshua Montroy [1], Rania Berjawi [1 2], Manoj M Lalu [1 3], Eyal Podolsky [1 2], Cayden Peixoto [2], Levent Sahin [1], Alain Stintzi [4], David Mack [5], Dean A Fergusson [6 7 8]

Results: 21 preclinical (n = 989 animals) and seven clinical (n = 164 patients) studies met eligibility. Preclinically, resistant starch was associated with a significant reduction in bowel mucosal damage compared to placebo (standardized mean difference - 1.83, 95% CI - 2.45 to - 1.20). Clinically, five studies reported data on clinical remission but clinical and methodological heterogeneity precluded pooling. In all five, a positive effect was seen in patients who consumed resistant starch supplemented diets. The majority of studies in both the preclinical and clinical settings were at a high or unclear risk of bias due to poor methodological reporting.

Conclusions: Our review demonstrates that resistant starch is associated with reduced histology damage in animal studies, and improvements in clinical remission in IBD patients. These results need to be tempered by the risk of bias of included studies. Rigorously designed preclinical and clinical studies are warranted. Trial registration The review protocols were registered on PROSPERO

Are all dietary fibers equal for patients with IBD?

› Nutr Rev. 2022 Apr 8;80(5):1179-1193. doi: 10.1093/nutrit/nuab062.

Are all dietary fibers equal for patients with inflammatory bowel disease? A systematic review of randomized controlled trials

Vera Peters [1], Gerard Dijkstra [1], Marjo J E Campmans-Kuijpers [1]

Affiliations + expand

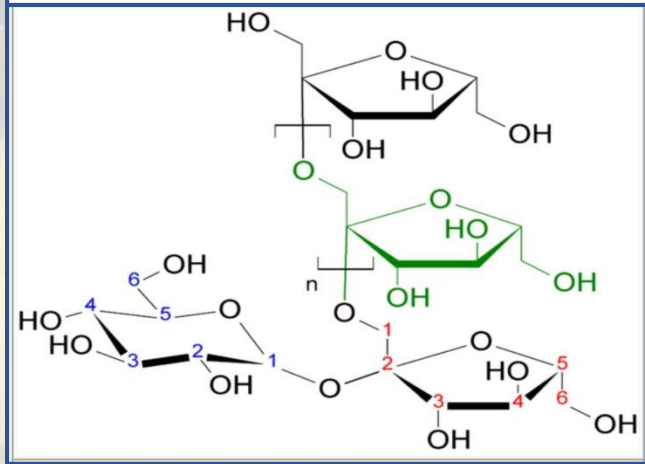
PMID: 34486663 PMCID: PMC8990763 DOI: 10.1093/nutrit/nuab062

Free PMC article

Conclusions: Although the evidence is sparse, **GBF and inulin seem propitious** and merit further exploration. Evidence on wheat bran and psyllium is still too limited. Adequately powered long-term human RCTs with objective outcomes are needed to improve dietary advice on types of fiber in IBD.

Inulin

- Inulin is a fructan
- Inulin enhances the growth of indigenous *Lactobacilli* and/or *Bifidobacteria*



Akram W, et al. Drug Discov Ther. 2019;13(1):1-8. doi: 10.5582/ddt.2019.01000.

Inuline studies bij mensen

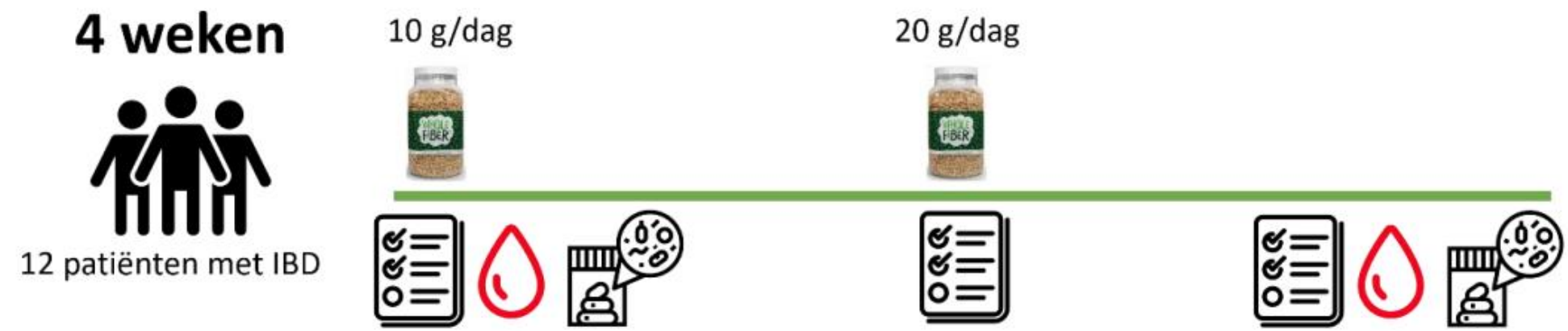
Clinical condition	Design	n	Treatment	Duration Treatment	Result
Chronic pouchitis[1]	Double-blind Placebo-controlled trial	20	Dietary inulin 24 g/d	6 week	Effective in the treatment of chronic pouchitis
Active CD[2]	Open-labeled trial	10	Oligofructose and inulin 15 g/d	3 week	Reduction of disease activity
Active UC[3]	Randomized, double-blinded controlled trial	18	Synbiotic	1 month	Reduction of inflammation

1. Welters CF, et al. Dis Colon Rectum. 2002; 45:621-627
2. Lindsay JO, et al. Gut. 2006; 55:348-355
3. Furrie E, et al. Gut. 2005; 54:242-249


Chicory root

WholeFiber study: Chic-IBD

Pilot naar het effect van prebiotische vezels op het darmmicrobioom en ontstekingswaarden bij mensen met ziekte van Crohn en Colitis Ulcerosa



Figuur 1 Studie design pilot patiënten met IBD

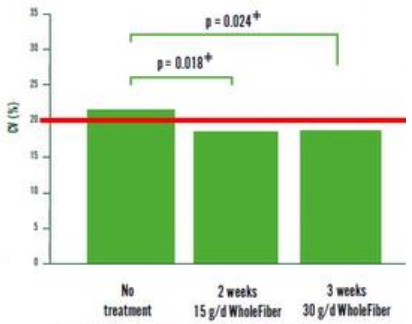
WholeFiber bij type 2 diabetes

Scientific evidence behind WholeFiber™

Daily consumption of WholeFiber™ had a clear health effect:

- ✓ Improved stool regularity
- ✓ Impact on the gut microbiota:
  - ✓ Increase in gut microbiota diversity and a 3-fold relative abundance of beneficial microbes such as *Bifidobacterium*
  - ✓ Increase in total short-chain fatty acid levels (+19%) and butyrate (+26%)
- ✓ Improved blood sugar levels in people at risk for type 2 diabetes[1]

Effect of WholeFiber on fecal acetate, propionate and butyrate. Increase compared to no treatment is shown in mM².



Coefficient of Variation (CV) of glucose level after WholeFiber intake as determined by Continuous Glucose Measurement (CGM)².

WholeFiber™ increased butyrate levels much more than extracted and purified inulin in colonic fermentations, while gas production was much lower², favoring WholeFiber™ over other prebiotic fibers.

[1]Puhlmann, M. L. et al (2022). *Dried chicory root improves bowel function, benefits intestinal microbial trophic chains and increases faecal and circulating short chain fatty acids in subjects at risk for type 2 diabetes.* Gut Microbiome; [2]ProDigest, in-house data, Gent, Belgium

GUT MICROBES
2021, VOL. 13, NO. 1, e1993582 (18 pages)
https://doi.org/10.1080/19490976.2021.1993582

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RESEARCH PAPER

OPEN ACCESS

Inulin-grown *Faecalibacterium prausnitzii* cross-feeds fructose to the human intestinal epithelium

Raphael R. Fagundes[a], Arno R. Bourgonje[a], Ali Saeed[a,e], Arnau Vich Vila[a,b], Niels Plomp[c], Tjasso Blokzijl[a], Mehdi Sadaghian Sadabad[c], Julius Z. H. von Martels[a], Sander S. van Leeuwen[d], Rinse K. Weersma[a,b], Gerard Dijkstra[a], Hermie J. M. Harmsen[b], and Klaas Nico Faber[a,d]

[a]Department of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [b]Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [c]Department of Medical Microbiology and Infection Prevention, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [d]Department of Laboratory Medicine, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands; [e]Institute of Molecular Biology & Biotechnology, Bahauddin Zakariya University, Multan, Pakistan

ABSTRACT

Many chronic diseases are associated with decreased abundance of the gut commensal *Faecalibacterium prausnitzii*. This strict anaerobe can grow on dietary fibers, e.g., prebiotics, and produce high levels of butyrate, often associated to epithelial metabolism and health. However, little is known about other *F. prausnitzii* metabolites that may affect the colonic epithelium. Here, we analyzed prebiotic cross-feeding between *F. prausnitzii* and intestinal epithelial (Caco-2) cells in a "Human-oxygen Bacteria-anaerobic" coculture system. Inulin-grown *F. prausnitzii* enhanced Caco-2 viability and suppressed inflammation- and oxidative stress-marker expression. Inulin-grown *F. prausnitzii* produced excess butyrate and fructose, but only fructose efficiently promoted Caco-2 growth. Finally, fecal microbial taxonomy analysis (16S sequencing) from healthy volunteers (n = 255) showed the strongest positive correlation for *F. prausnitzii* abundance and stool fructose levels. We show that fructose, produced and accumulated in a fiber-rich colonic environment, supports colonic epithelium growth, while butyrate does not.

ARTICLE HISTORY
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KEYWORDS
Gut bacteria; dysbiosis; fructose; intestinal epithelium; Faecalibacterium; inulin

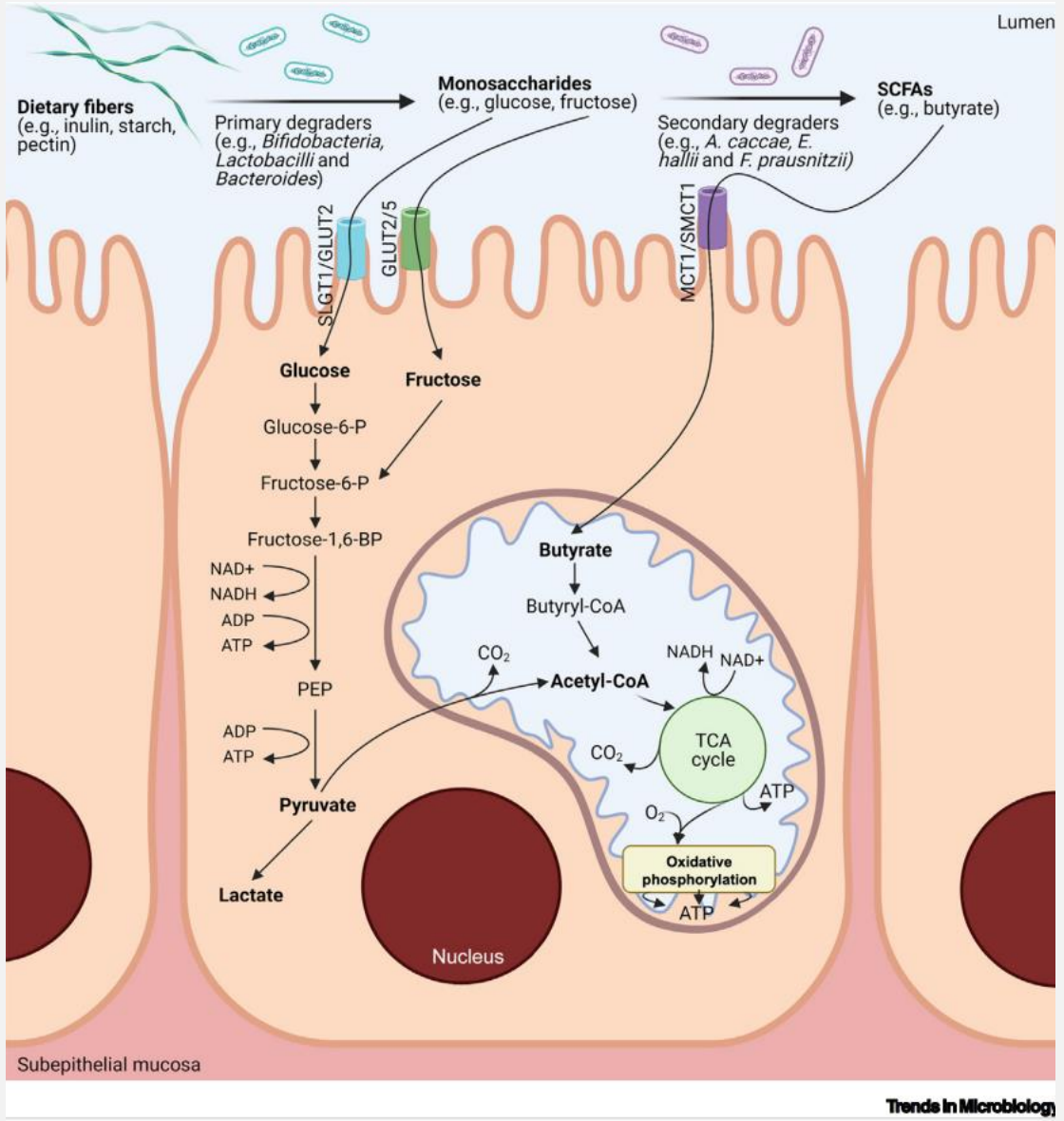
Trends in Microbiology

CellPress OPEN ACCESS

Review

Beyond butyrate: microbial fiber metabolism supporting colonic epithelial homeostasis

Raphael R. Fagundes,[1] Saskia C. Belt,[1] Barbara M. Bakker,[2] Gerard Dijkstra,[1] Hermie J.M. Harmsen,[3] and Klaas Nico Faber[1,*]



Gastroenterology 2023;164:228–240

INFLAMMATORY BOWEL DISEASE

Unfermented β-fructan Fibers Fuel Inflammation in Select Inflammatory Bowel Disease Patients

Heather K. Armstrong,[1,2,3] Michael Bording-Jorgensen,[1,2] Deanna M. Santer,[4]

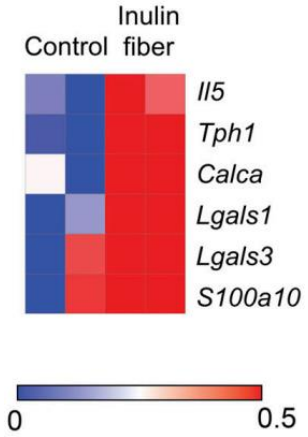
: Unfermented dietary b-fructan fibers induced proinflammatory cytokines in a subset of IBD intestinal biopsies cultured ex vivo, and immune cells (including peripheral blood mononuclear cells). Results were validated in an adult IBD randomized controlled trial examining bfructan supplementation. The proinflammatory response to intact b-fructan required activation of the NLRP3 and TLR2 pathways. Fermentation of b-fructans by human gut whole microbiota cultures reduced the proinflammatory response, but only when microbes were collected from patients without IBD or patients with inactive IBD. Fiber-induced immune responses correlated with microbe functions, luminal metabolites, and dietary fiber avoidance. CONCLUSION: Although fibers are typically beneficial in individuals with normal microbial fermentative potential, some dietary fibers have detrimental effects in select patients with active IBD who lack fermentative microbe activities. The study is publicly accessible at the U.S. National Institutes of Health database (clinicaltrials.gov identification number NCT02865707).

JEM Journal of Experimental Medicine

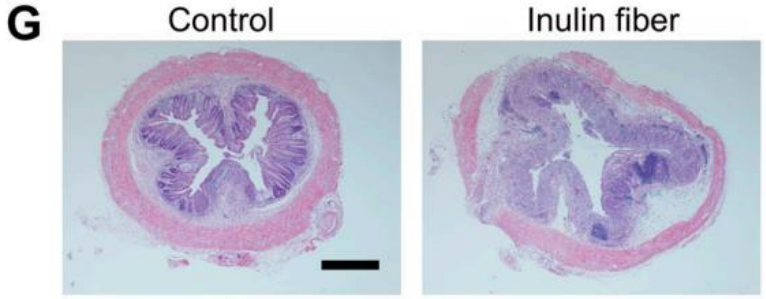
ARTICLE

Dietary fiber is a critical determinant of pathologic ILC2 responses and intestinal inflammation

Mohammad Arifuzzaman[1,2,3,4], Tae Hyung Won[7], Hiroshi Yano[1,2,3,4], Jazib Uddin[1,2,3,4], Elizabeth R. Emanuel[1,2,3,4,5], Elin Hu[1,2,3,4], Wen Zhang[1,2,3,4], Ting-Ting Li[1,2,3,4], Wen-Bing Jin[1,2,3,4], Alex Grier[1,2,3,4], Sanchita Kashyap[1,2,3,4], JRI Live Cell Bank[1], Chun-Jun Guo[1,2,3,4], Frank C. Schroeder[7], and David Artis[1,2,3,4,5,6]



Innate lymphoid cells (ILCs) can promote host defense, chronic inflammation, or tissue protection and are regulated by cytokines and neuropeptides. However, their regulation by diet and microbiota-derived signals remains unclear. We show that an inulin fiber diet promotes *Tph1*-expressing inflammatory ILC2s (ILC2^{INFLAM}) in the colon, which produce IL-5 but not tissue-protective amphiregulin (AREG), resulting in the accumulation of eosinophils. This exacerbates inflammation in a murine model of intestinal damage and inflammation in an ILC2- and eosinophil-dependent manner. Mechanistically, the inulin fiber diet elevated microbiota-derived bile acids, including cholic acid (CA) that induced expression of ILC2-activating IL-33. In IBD patients, bile acids, their receptor farnesoid X receptor (FXR), IL-33, and eosinophils were all upregulated compared with controls, implicating this diet–microbiota–ILC2 axis in human IBD pathogenesis. Together, these data reveal that dietary fiber–induced changes in microbial metabolites operate as a rheostat that governs protective versus pathologic ILC2 responses with relevance to precision nutrition for inflammatory diseases.

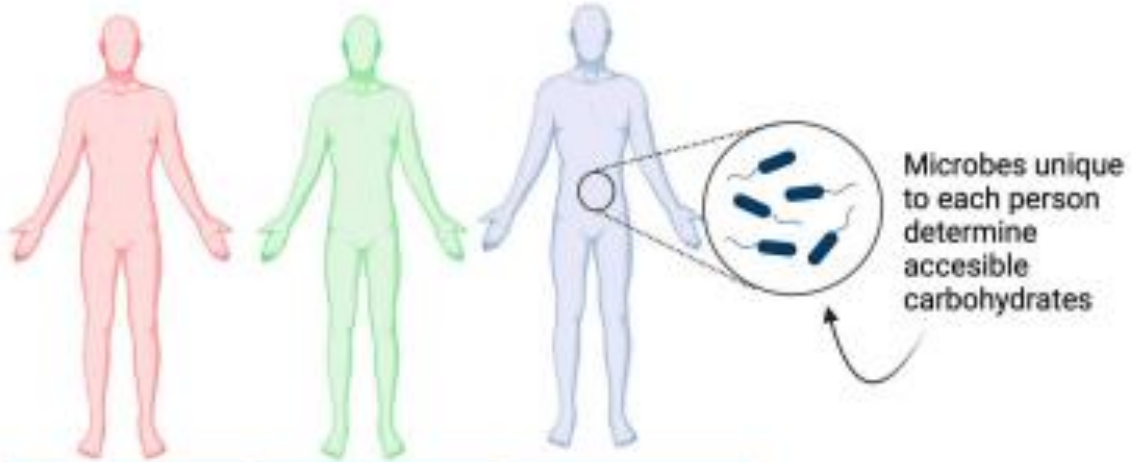


Conclusie van fructan studies

- Gezonde mensen: ↑ *Bifidobacterium*
- CD: ↑ *Bifidobacterium* & SCFA, ↓ disease activity
- UC: ↑ butyrate, ↑ SCFA levels, ↓ calprotectin
- actieve IBD: kan schadelijke effecten hebben

1. Joossens, 2011
2. De Preter, 2013
3. Joossens 2012
4. Lindsay, 2006
5. Benjamin 2011
6. Casellas, 2007
7. Alles 1997
8. Armstrong, 2023

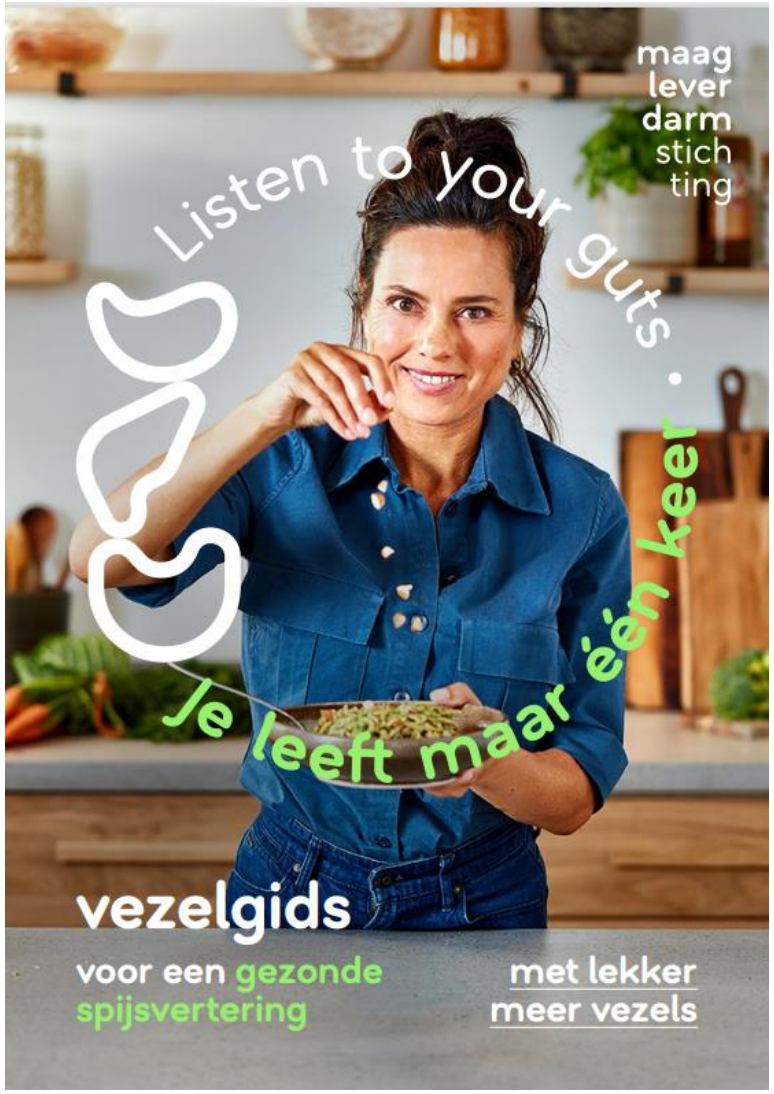
Personalized diet



		Source	Person A		Person B		Person C	
			MAC	Diet	MAC	Diet	MAC	Diet
High SCFAs	Pectin	Orange	X	✓	X	✓	✓	X
	Resistant Starch	Potato	X	✓	✓	✓	X	X
	B glucan	Oats	X	✓	✓	✓	X	X
Low SCFAs	Mucin		✓		X		X	
	Mucous Thickness		Thin Mucous		Thick Mucous		Normal Mucous	
	Regulatory T Cells		Few		Many		Few	
	Intervention		Improve the Microbiome		None Necessary		Dietary Intervention	

Bron: Haskey N, et al To Fiber or Not to Fiber: The Swinging Pendulum of Fiber Supplementation in Patients with Inflammatory Bowel Disease. Nutrients. 2023 Feb 21;15(5):1080. doi: 10.3390/nu15051080. PMID: 36904081;

Hoe kies je voor meer vezels?



Lage en hoge vezel inname

		vezel				vezel
75 g	witbrood	1.8 g	**Ontbijt/ Lunch**	75 g	volkoren brood	4.8 g
25 g	cornflakes	0.8 g		50 g	fruit muesli	4.3 g
45 g	wit bolletje	1.7 g		45 g	donker roggebrood	3.7 g
10 g	beschuit	0.3 g		10 g	volkoren knäckebröd	1.4 g
	boter				boter	
	kaas			20 g	hummus	1.5 g
15 g	marmelade	0.2 g		15 g	pindakaas	1.6 g
200 g	noodle soep	1.8 g		200 g	erwtensoep soep	7.0 g
200 g	sinaasappelsap	0.6 g		150 g	sinaasappel	2.6 g
10 g	biscuit	0.3 g	**Snack**	25 g	noten	1.5 g
200 g	sinaasappelsap	0.6 g		150 g	appel	2.7 g
220 g	witte rijst	1.5 g	**Diner**	240 g	volkoren rijst	5.0 g
100 g	varkenslapje			100 g	quorn	5.5 g
150 g	komkommer	0.5 g		150 g	groente	3.5 g
	Total	**10.1 g**			**Total**	**45.1 g**

Dr. Marjo Campmans-Kuijpers

Conclusie: voedingsvezel in algemeen

- Er zijn verschillende soorten voedingsvezel
- Consensus nodig over de definitie van voedingsvezel en over de aanbevelingen
- Inname voedingsvezel is veel minder dan de aanbevolen hoeveelheden
- Nauwelijks richtlijnen over soorten voedingsvezel en soorten voedingsmiddelen
- Onderzoek naar verschillende typen voedingsvezel en hun lange-termijn effect is nodig

Conclusie: voor IBD

- Voedingsvezels zorgt vaak voor verbetering, maar laat niet consistent vermindering van symptomen of remissie zien bij IBD patiënten
- Meer voedingsvezel is niet gunstig voor **alle** IBD patiënten
- Resultaten zijn afhankelijk van:
  - Ziekte activiteit
  - Intact colon
  - Microbioom samenstelling

Bedankt voor jullie aandacht!

Vragen?

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