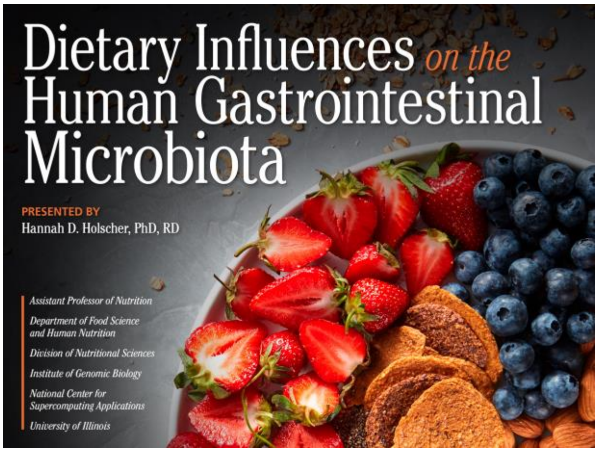


Learning Objectives

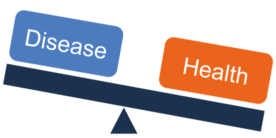
- Identify dietary factors that impact the human gastrointestinal (GI) microbiota.
- Compare and contract how different types of foods, which contain fiber, differentially impact the GI microbiota.
- Establish a connection between the GI microbiota and health.

2

Definitions and Overview

Microbiome *- a collection of microbial genomes*
Microbiota *– a collection of microbes*

- **As many bacteria** as host cells in human body[1]
- \> **150x more bacterial** genes than our human genome[2]



1. Sender, R., et al. (2016). Are we really vastly outnumbered? Revisiting the ratio of bacterial to host cells in humans. *Cell*, 164(3), 337-340.
2. Qin, J., et al. (2010). A human gut microbial gene catalog established by metagenomic sequencing. *Nature*, 464(7285), 59.

3

Definitions: Fiber & Prebiotic

Dietary Fiber: *Non-digestible soluble and insoluble carbohydrates ($\geq$ 3 monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates ($\geq$ 3 or more monomeric units) determined by FDA to have* ***physiological effects that are beneficial to human health****.*[1]

Prebiotic: *A substrate that is selectively utilized by host microorganisms* ***conferring a health benefit****.*[2]

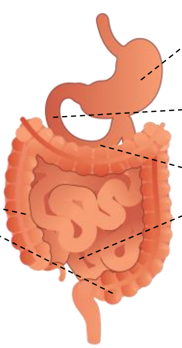
1. U.S. Food & Drug Administration, 26 May 2017. Final ruling on dietary fiber definition.
2. Gibson, G. R., et al. (2017). Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nature Reviews Gastroenterology & Hepatology*. 2017. 14(8): 491-502

Diet & GI Microbiota

- The composition of the diet impacts ***digestive secretions***, ***transit time***, and ***absorption.***
- Diet provides a ***source of nutrients*** for us and the GI microbiota.
- Diet provides a ***source of microbes.***

Diet, GI Physiology, & Microbiota

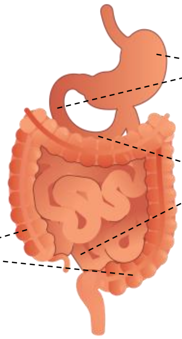
Nutrient composition affects GI secretions & transit time



Diet, GI Physiology, & Microbiota

Diet affects GI microbiota composition

Colon
$10^{10} – 10^{12}$ CFU/mL
Bacteroides
Prevotella
Facaelibacterium
Ruminococcus
Roseburia
Clostridium
Bifidobacteria
Collinsella
Desulfovibrio
Bilophila
Akkermansia
Methanobrevibacter

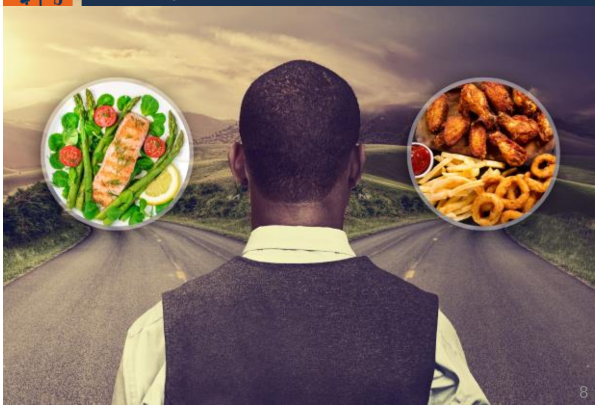


Stomach & Duodenum
$10^{1}– 10^{2}$ CFU/mL
Helicobacter
Streptococcus

Jejunum & Ileum
$10^{4} – 10^{8}$ CFU/mL
Bacteroides
Streptococcus
Lactobacillius
Bifidobacteria
Fusobacteria

7

A Deeper Dive Into Diet & Microbiota



8

Diet Impacts GI Microbiota

- ***Habitual diet*** is related to the composition of the GI microbiota.[1]
- ***Acute changes*** in macronutrient composition can rapidly (within 2-4 days) change the composition and function of gut microbes.[2]
- Individuals that consume ***more plants*** have greater GI bacterial diversity.[3]
- ***Dietary fiber and prebiotic*** intake differentially impacts GI microbiota composition and function.[4]

1. Wu, G. D., et al. (2011). Linking long-term dietary patterns with gut microbial enterotypes. *Science*, *334*(6052), 105-108.
2. David, L. A., et al. (2014). Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, *505*(7484), 559-563.
3. McDonald D., et al (2018). American Gut: an open platform for citizen science microbiome research. *mSystems*, 3(3) e00031-18
4. Holscher, H. D. (2017). Dietary fiber and prebiotics and the gastrointestinal microbiota. *Gut Microbes*, 8(2), 172-184.

9

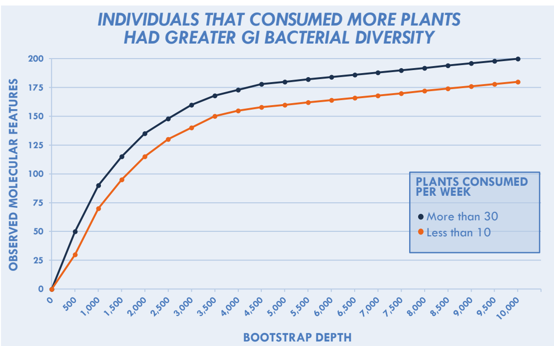
Diet & GI Microbiota

- Cross-sectional analysis of > 10,000 fecal samples from participants in the US, UK, and Australia
- Individuals completed health status and dietary questionnaires

McDonald D., et al (2018). American Gut: an open platform for citizen science microbiome research. *mSystems*, 3(3) e00031-18

10

Plants & Microbiota Diversity



McDonald D, (2018). American Gut: an open platform for citizen science microbiome research. *mSystems*, 3(3) e00031-18

11

Dietary Fibers in Foods

Common Dietary Plants

Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

12

Dietary Fibers in Foods

Common Dietary Plants

- Brans, Cereals, Legumes, Nuts, Peas
- Brans, Cereal grains, Legumes, Nuts, Vegetables, Fruit
- Oats, Barley, Rye
- Fruits, Vegetables, Legumes, Potato, Sugar beets
- Chicory root, Onion, Agave, Wheat, Bananas, Garlic

Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

13

Dietary Fibers in Foods

Common Dietary Plants

- Brans, Cereals, Legumes, Nuts, Peas
- Brans, Cereal grains, Legumes, Nuts, Vegetables, Fruit
- Oats, Barley, Rye
- Fruits, Vegetables, Legumes, Potato, Sugar beets
- Chicory root, Onion, Agave, Wheat, Bananas, Garlic

Which type of fibers are in these foods?

Fructans, pectins, cellulose, β-glucans, hemicelluloses

Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

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Dietary Fibers in Foods

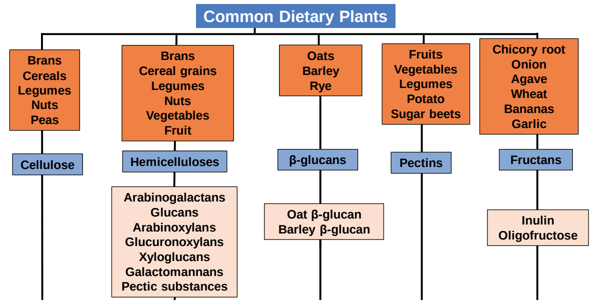
Common Dietary Plants

- Brans, Cereals, Legumes, Nuts, Peas → Cellulose
- Brans, Cereal grains, Legumes, Nuts, Vegetables, Fruit → Hemicelluloses
- Oats, Barley, Rye → β-glucans
- Fruits, Vegetables, Legumes, Potato, Sugar beets → Pectins
- Chicory root, Onion, Agave, Wheat, Bananas, Garlic → Fructans

Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

15

Dietary Fibers in Foods



Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

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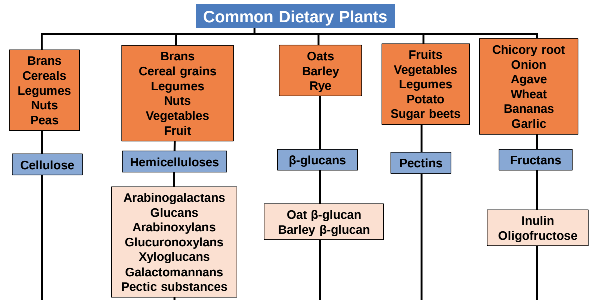
Dietary Fibers in Foods



Which of these are **fermentable? Soluble? Insoluble? Viscous?**

Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

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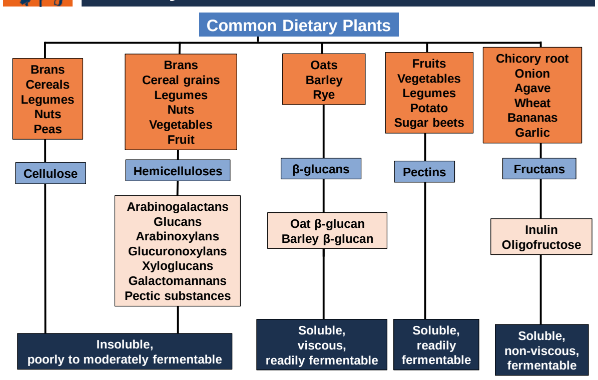
Dietary Fibers in Foods



Livingston KA, Chung M, Sawicki CM, Lyle BJ, Wang DD, Roberts SB, et al. (2016) Development of a Publicly Available, Comprehensive Database of Fiber and Health Outcomes: Rationale and Methods. PLoS ONE 11(6): e0156961.

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Dietary Fiber Health Benefits

- ***Insoluble (cellulose, bran)***
  - Laxative effect
- ***Soluble, viscous, non-fermented (psyllium)***
  - Cholesterol-lowering, improve glycemia, weight loss, stool normalization
- ***Soluble, viscous, readily fermented (β-glucan, pectin)***
  - Cholesterol-lowering, improve glycemia

McRoie JW & Fahey GC. (2013). A review of gastrointestinal physiology and the mechanisms underlying the health benefits of dietary fiber: Matching an effective fiber with specific patient needs. *Clinical Nursing Studies*, *1*(4), 82-92.

19

Dietary Fiber Health Benefits

- ***Soluble, non-viscous, fermentable***:
  - Fructooligosaccharides (FOS)
  - Galactooligosaccharides (GOS)
  - Inulin
  - Polydextrose
- Accumulating data on health benefits

McRoie JW & Fahey GC. (2013). A review of gastrointestinal physiology and the mechanisms underlying the health benefits of dietary fiber: Matching an effective fiber with specific patient needs. *Clinical Nursing Studies*, *1*(4), 82-92.

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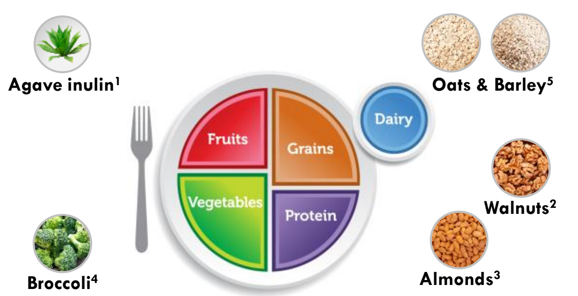
Diet & GI Microbiota

Dietary intervention trials allow for characterization of the impact of foods on the GI microbiota



1. Holscher HD, et al., *J. Nutr* 2015; 2. Holscher HD, et al., *J. Nutr* 2018 3. Holscher HD, et al., *Nutrients* 2018; 4. Kaczmarek JL, et al., *J. Nutr Bioc 2018; 5. Thompson, S.V et al., FASEB 2016; 6. image:* U.S. Department of Agriculture myPlate

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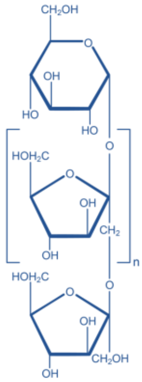
Inulin Type Fibers

Plant Sources
- Wheat
- Bananas
- Garlic
- Onion
- Agave
- Chicory root

Food Sources
- Bars
- Cereals
- Yogurt
- Ice cream



- ***Structures***
  - Fructose polymer linked by β-2,1 linkages
  - Varying degrees of polymerization (2-60)
  - Fructooligosaccharides (FOS) → Inulin

Meyer TSM (2015). Biotechnological Production of Oligosaccharides — Applications in the Food Industry, Food Production and Industry. DOI: 10.5772/60934.

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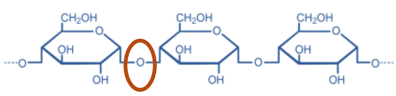
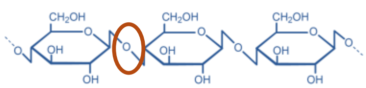
Microbes Ferment Dietary Fiber

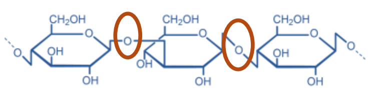
Microbes Ferment Dietary Fiber



Amylose: α-1,4 glucosidic bonds



Cellulose: β-1,4 glucosidic bonds



β-Glucan: *mixed β-1,3 and β-1,4 glucosidic bonds*

Image adapted from Linus Pauling Institute, OSU

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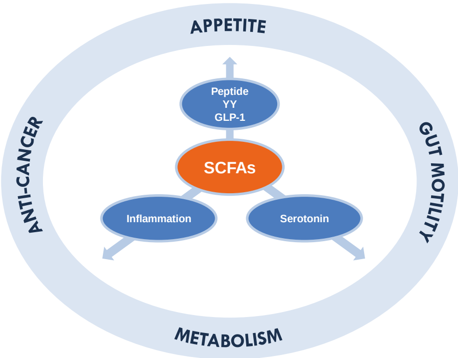
Microbiota-Derived Signaling



Evans, James M., Laura S. Morris, and Julian R. Marchesi. *Journal of Endocrinology* 218.3 (2013): R37-R47.

25

Inulin Type Fibers & Microbiota

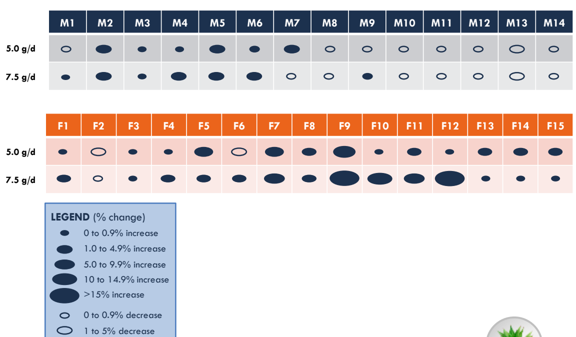
Microbial

- 16 g/d inulin and oligofructose (50/50) for 12 wk increased ***Bifidobacteria spp.*** *and* ***Faecalibacterium prausnitzii***[1]
- 5 & 7.5 g/d agave inulin increased ***Bifidobacteria*** **spp.** and **SCFA**[2]
- Positive relations between ***Faecalibacterium*** **spp.** and **butyrate** concentrations[2]
- 12 g/d inulin increased ***Bifidobacteria spp.*** and decreased ***Bilophila spp.***, no change in SCFA[1]

1. Dewulf EM (2013). Insight into the prebiotic concept: lessons from an exploratory, double-blind intervention study with inulin-type fructans in obese women. *Gut*; 62: 1112-21.
2. Holscher HD (2015) Agave Inulin Supplementation Affects the Fecal Microbiota of Healthy Adults Participating in a Randomized, Double-Blind, Placebo-Controlled, Crossover Trial. *J Nutr*; 145:2025–32

26

Inulin: Phenotypic Responses



Holscher, H. D., et al. (2015). Agave inulin supplementation affects the fecal microbiota of healthy adults participating in a randomized, double-blind, placebo-controlled, crossover trial. *The Journal of Nutrition*, *145*(9), 2025-2032.

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Inulin-Type Fibers & Health

- ***Immunomodulation***
  - Reduced high-sensitivity CRP, IL-6 and/or TNF-α, and endotoxin[1]
  - 10 g/d for 60 days decreased IL-6 and TNF-α [2]
- ***Appetite and Food Intake***
  - 21 g/d for 12 wk increased PYY, decreased ghrelin, and reduced food intake.[3]
  - 16 g/d for 2 wk increased plasma glucagon-like peptide 1 and PYY.[4]
- ***Body Composition***
  - 21 g/d oligofructose for 12 wk reduced body weight, fat mass and trunk fat.[3]
  - 16 g/d combination of inulin and oligofructose for 12 wk did not change body composition, fat mass tended to decrease.[5]
- ***Glycemia***
  - 16 g/d for 2 wk decreased postprandial glucose responses after a meal.[4]

1. Fernandes R, et al. (2016). Effects of inulin-type fructans, galacto-oligosaccharides and related synbiotics on inflammatory markers in adult patients with overweight or obesity: A systematic review. *Clinical Nutrition;* 36(5): 1197-1206
2. Dehghan P, et al. (2014) Oligofructose-enriched inulin improves some inflammatory markers and metabolic endotoxemia in women with type 2 diabetes mellitus: a randomized controlled clinical trial. *Nutrition*; 30: 418–23.
3. Parnell JA. Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. *AJCN* 2009; 89:1751–59.
4. Cani PD, et al. (2009). Gut microbiota fermentation of prebiotics increases satietogenic and incretin gut peptide production with consequences for appetite sensation and glucose response after a meal. *AJCN,* 90(5), 1236-43.
5. Dewulf EM, et al. Insight into the prebiotic concept: lessons from an exploratory, double-blind intervention study with inulin-type fructans in obese women. Gut 2013; 62: 1112-21.

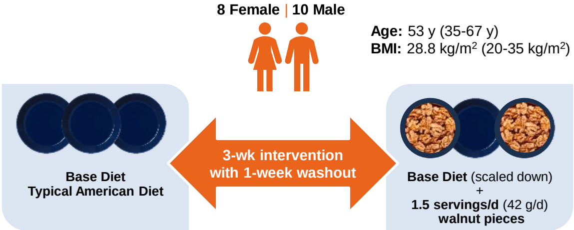
28

Walnuts

Randomized, controlled, cross-over design

8 Female | **10 Male**

Age: 53 y (35-67 y)
BMI: 28.8 kg/m² (20-35 kg/m²)



Holscher HD, et al., Walnut consumption alters the gastrointestinal microbiota, microbially derived secondary bile acids, and health markers in healthy adults: a randomized controlled trial *J. Nutr* 2018; 148 (6): 861-867

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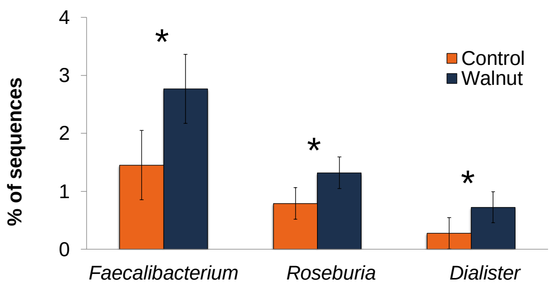
Walnuts Impacted GI Microbiota

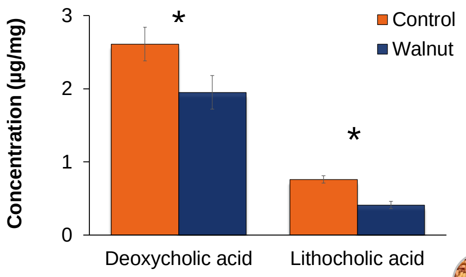


*P<0.05

Holscher HD, et al., *J. Nutr* 2018

30

Walnuts Reduced Secondary Bile Acids



*P<0.05

Holscher HD, et al., *J. Nutr* 2018

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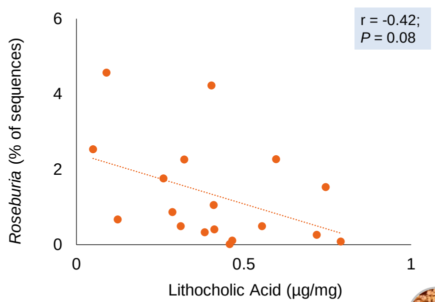
Walnuts Reduced Secondary Bile Acids



Holscher HD, et al., *J. Nutr* 2018

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Almonds

Randomized, controlled, cross-over design

n=18
Age: 57 y (33-72 y)
BMI: 30 kg/m2 (22-36 kg/m2)

3 Week Treatment

Control | Whole Almonds | Roasted Almonds | Chopped Almonds | Almond Butter

Wash Out Period

Holscher HD, et al., Almond consumption and processing affects the composition of the gastrointestinal microbiota of healthy adult men and women: a randomized controlled trial. *Nutrients* 2018; 10 (2): 126

33

Almonds

Randomized, controlled, cross-over design

n=18
Age: 57 y (33-72 y)
BMI: 30 kg/m2 (22-36 kg/m2)

3 Week Treatment

Wash Out Period

Roasted Almonds | Control | Chopped Almonds | Almond Butter | Whole Almonds

Holscher HD, et al., Almond consumption and processing affects the composition of the gastrointestinal microbiota of healthy adult men and women: a randomized controlled trial. *Nutrients* 2018; 10 (2): 126

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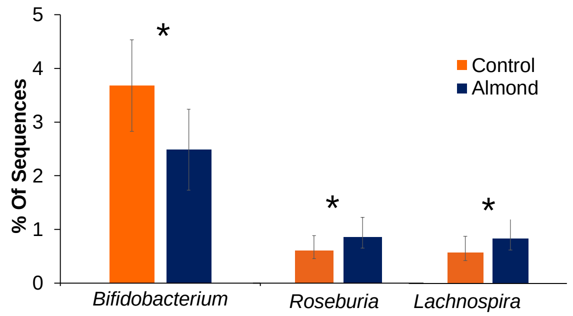
Almonds Impact GI Microbiota



*P<0.05

Holscher HD, et al., *Nutrients* 2018

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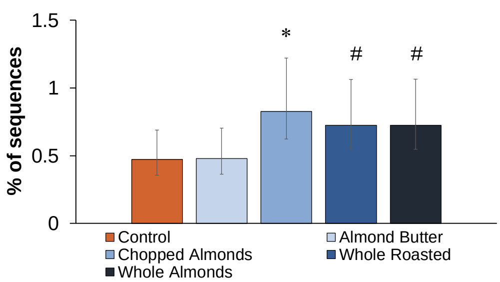
Chopped Almonds Increased *Roseburia*



*P<0.05

Holscher HD, et al., *Nutrients* 2018

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Broccoli & GI Microbiota

Randomized, controlled, cross-over design

Healthy Adults
N=18

Age (y)=57 (37-65)
BMI (kg/m²)=26.2 (19.0-36.6)

INTERVENTION
200 g Broccoli + 20 g radish
16 days

CONTROL
0 g Broccoli/radish
16 days

14 DAY WASHOUT

INTERVENTION
200 g Broccoli + 20 g radish
16 days

CONTROL
0 g Broccoli/radish
16 days

Kaczmarek JL, et al., Broccoli consumption affects the human gastrointestinal microbiota *J Nutr Bioc* 2019; 63: 27-34

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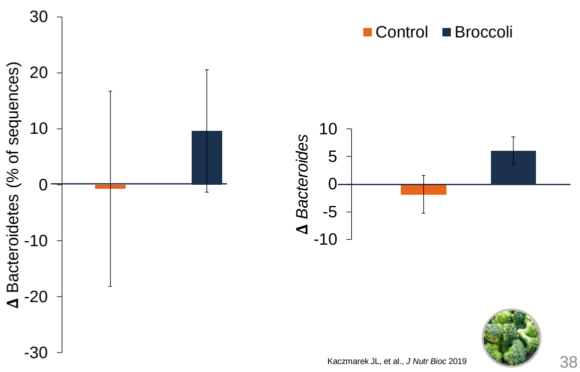
Broccoli Increased *Bacteroides*



Kaczmarek JL, et al., *J Nutr Bioc* 2019

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Whole Grain Oats & Barley

- **7-day menu cycle** of standard American diet items
- **Treatments included** cereal, granola, trail mix, and fruit cereal bars

Healthy Adults (n=68)

CONTROL (n=21)	OATS (n=23)	BARLEY (n=24)
Baseline Visit	Baseline Visit	Baseline Visit
0.8 servings per 1800kcal	4.4 servings per 1800kcal	4.4 servings per 1800kcal
Post-Treatment Visit	Post Treatment Visit	Post Treatment Visit

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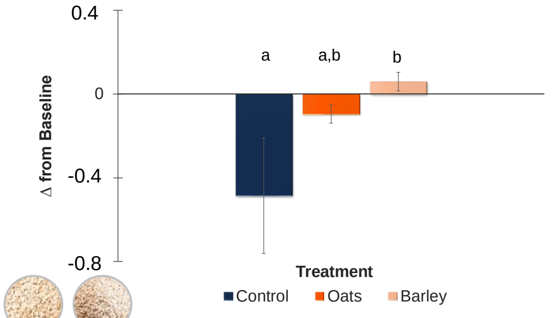
Whole Grain Barley Increased *Roseburia*



Thompson, S.V et al., *FASEB* 2016

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Which macronutrients can impact the GI microbiota?

	% Daily Value*
Total Fat 4g	**6%**
Saturated Fat 2g	**10%**
Trans Fat 0g	
Polyunsaturated Fat 0g	
Monounsaturated Fat 0g	
Cholesterol 0mg	**0%**
Sodium 120mg	**5%**
Potassium 160mg	**5%**
Total Carbohydrate 44g	**15%**
Dietary Fiber 8g	**33%**
Soluble Fiber 5g	
Insoluble Fiber 3g	
Sugars 12g	
Protein 4g	
Vitamin A 0% **Vitamin C** 10%	
Calcium 0% **Iron** 8%	

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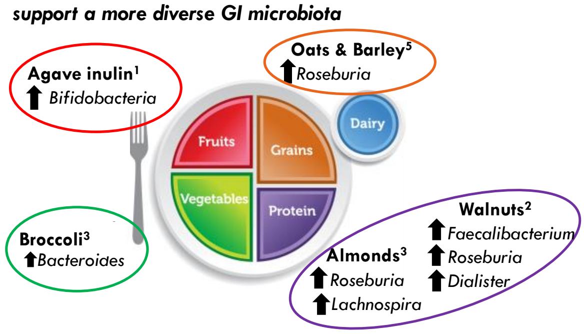
Diet & GI Microbiota

Eating a diet rich in different types and sources of fibers helps support a more diverse GI microbiota



1. Holscher HD, et al., *J. Nutr* 2015; 2. Holscher HD, et al., *J. Nutr* 2018 3. Holscher HD, et al., *Nutrients* 2018; 4. Kaczmarek JL, et al., *J. Nutr Bioc 2018; 5. Thompson, S.V et al., FASEB 2016; 6. image:* U.S. Department of Agriculture myPlate

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Diet & GI Microbiota

Agave inulin[1]
⬆ *Bifidobacteria*

Oats & Barley[5]
⬆ *Roseburia*

Food (fiber) source, dose, & form matter

Broccoli[4]
⬆ *Bacteroides*

Walnuts[2]
⬆ *Faecalibacterium*
⬆ *Roseburia*
⬆ *Dialister*

Almonds[3]
⬆ *Roseburia*
⬆ *Lachnospira*

1. Holscher HD, et al., *J. Nutr* 2015; 2. Holscher HD, et al., *J. Nutr* 2018 3. Holscher HD, et al., *Nutrients* 2018; 4. Kaczmarek JL, et al., *J. Nutr Bioc 2018; 5. Thompson, S.V et al., FASEB 2016*

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Key Takeaways

1
Diet impacts the human GI microbiota.

2
Consumption of different types of ***foods, which contain fiber,*** differentially impact the GI microbiota.

3
Increasingly, microbes and microbial metabolites are linked to ***human health.***

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Acknowledgements

Collaborators: George Fahey, PhD, Elizabeth Jeffery, PhD, Kelly Swanson, PhD, Michael Miller, PhD, David Baer, PhD, Janet Novotny, PhD, Craig Charron, PhD, American Gut Consortium

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Other Funding & Honoria: Academy of Nutrition and Dietetics, Hass Avocado Board, Foundation for Food and Agriculture Research, Egg Nutrition Council, Abbott Nutrition, National Cattlemen's Beef Association, Nutrition North America

Questions

Dr. Holscher is an assistant professor of nutrition in the Department of Food Science and Human Nutrition, and a member of the Division of Nutritional Sciences, the Institute of Genomic Biology, and the National Center for Supercomputing Applications at the University of Illinois, where she has been a faculty member since 2015. Before joining the faculty, she completed postdoctoral training focused on the human microbiome, as well as a Ph.D. in Nutritional Sciences and a B.S. in Food Science and Human Nutrition at the University of Illinois. She is also a Registered Dietitian. Research in Dr. Holscher's laboratory, the *Nutrition and Human Microbiome Laboratory*, integrates the areas of nutrition, gastrointestinal physiology, and the microbiome. Her research focuses on the clinical application of nutritional sciences with an overarching goal of improving human health through dietary modulation of the gastrointestinal microbiome.

Website: https://hdh.fshn.illinois.edu/

Twitter: @HolscherLab

Nutrition & Human Microbiome Laboratory

Credit Claiming

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