

PHGG: Effects on gut ecosystem and clinical benefits

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Disclosure: She has certified that no conflict of interest exists for this presentation.



Competing interests

Dr. Slavin thanks the following organizations for providing research funds for her laboratory the past 5 years. American Pulse Association, ILSI-NA, MNDrive Global Food Ventures, United States Department of Agriculture, the Mushroom Council, GSK, Pepsico, Ingredion, Coca-Cola, Danone, Welch's, Nestle Health Sciences, DSM, Nexira and Taiyo.

These research projects are in the areas of dietary fiber, whole grains, legumes, FODMAPS, nutrient losses in deep winter greenhouses, mushrooms, digestive health, protein needs, carbohydrate needs, and snacking.

She serves on the scientific advisory board for Tate and Lyle and Atkins Nutritionals.

She owns a 1/3 share of the Slavin Sisters Farm LLC, a 119 acre farm in Walworth, Wisconsin.



Learning Objectives

- 1. Discuss the latest science behind recommendations for dietary fiber and prebiotics.
- 2. Update new research on the physiological effects of dietary fibers, with an emphasis on partially hydrolyzed guar gum (PHGG).
- 3. Describe the prebiotic benefits of PHGG, including additional effects on the gut ecosystem.
- Identify regulations around the world that limit acceptance of changes in the gut microbiota to health outcomes.



Fiber agreement

- Marker of a healthy diet
 - Recommend whole grains, fruits, vegetables, legumes
- Concept
 - carbohydrates and lignin that escape digestion in the upper GI tract but may be fermented in the gut
- Nutrient
 - according to 2002 Dietary Reference Intakes (DRIs)
- Regulated
 - On the Nutrition Facts panel 25 g current Daily Value (DV), proposed to increase to 28 g DV
- Health claims
 - oat bran, barley bran, and psyllium and CVD in US

Relative Risk of Death From Coronary Heart Disease





Fiber: Effects throughout the GI tract

Delayed nutrient absorption, blunted glucose and insulin response

Change in gut hormones (GLP-1, PYY, ghrelin)





Changing fiber regulations by the FDA

- Fiber definition will now require each isolated and synthetic fiber (functional fiber) to have a proven health benefit
 - Qualifying health benefits include
 - Lowering blood glucose and cholesterol levels
 - Lowering blood pressure
 - Improved laxation
 - Increase mineral absorption
 - Reduced energy intake
 - Changes in specific GI taxa are not considered a direct health benefit



Fibers that Meet the Dietary Fiber Definition

- β-glucan soluble fiber(as described in § 101.81(c)(2)(ii)(A)) (AOAC 992.28)
- Psyllium husk (as described in 101.81(c)(2)(ii)(A)(6)) (AOAC 991.43)
- Cellulose
- Guar gum
- Locust bean gum
- Pectin
- Hydroxypropylmethylcellulose



Additional fibers accepted by FDA

- Mixed plant cell wall fibers
- Arabinoxylan
- Inulin and inulin-type fructans
- High amylose starch (RS2)
- Galactooligosaccharide
- Polydextrose
- Resistant maltodextrin/dextrin



Challenges for new fibers

- Most intact and intrinsic fibers (grains, vegetables, fruits, pulses) are not functional – they are not water soluble, not stable in a wide range of pH and temperature, taste bad, are grainy, etc.
- Clean label demands limit consumer acceptance of fibers that sound "chemical"
- New FDA regulations require extensive clinical studies to be accepted as a dietary fiber
- Without that approval, you can be added to foods, beverages, supplements, but can't be claimed as a fiber source









Guar Seeds, Cultivated in India

Guar Plant *Cyamopsis tetragonolobus*



Manufacturing Process of PHGG



Partially Hydrolyzed Guar Gum (PHGG), a water-soluble dietary fiber produced by a controlled partial enzymatic hydrolysis of guar beans.





Fiber in the human gut

- Fibers (pectin, inulin) can be extensively fermented (> 90%) or poorly fermented (purified cellulose, <10%)
- Even fibers that are extensively fermented can increase fecal biomass since bacterial mass increases and that also binds water
- Feces are about 75% water so surviving fiber or bacteria will increase fecal weight



Fiber and laxation

- Different fibers have different effects on stool weight, but a properly powered study will show differences in stool weight with fiber intake
- Stool frequency generally does not change if frequency is already normal (1/day)
- If transit time is normal (2 days, 48 hours), additional fiber will not change transit time (Marlett et al. *Am J Clin Nutr* 2000;72:784-789).
- Fiber intakes will normalize transit times to 2 4 days (Harvey et al. *Lancet* 1973;1:1278-1280).



Fermentation by microflora

- Some evidence suggests fiber fermentation provides physiological benefit such as
 - Increased mineral absorption
 - Stimulation of beneficial microbes (prebiotic)
 - Decrease survival of pathogenic bacteria through reduction in pH
 - Providing nourishment to colonocytes (SCFAs, butyrate) for increased cell growth & maintenance



Limitations to fecal samples

- Not practical in epidemiological studies
- No accepted standard
 - Stool weight
 - Stool chemistry
 - Microflora methods, what is best
 - Stool frequency (easy to collect)
 - Quality of life (used in IBS trials)



Short Chain Fatty Acids (SCFA)



SCFA are organic acids such as acetic, propionic, and butyric acids.

Bacterial fermentation of fiber in the large intestine leads to production of short chain fatty acids (SCFA).



Excellent Physiological Effects of Short Chain Fatty Acids (SCFA)

Influence of SCFA on Intestinal Growth and Function

- Enhancement of mucosal blood flow in large intestine.
- · Enhancement of epithelial cell proliferation in large intestine.
- Enhancement of water, Ca and Mg absorption in large intestine.
- Enhancement of mucus secretion in large intestine.



Total Short Chain Fatty Acid Production



Total SCFA (acetate + propionate + butyrate + isobutyrate)





Dietary components that alter gut bacteria

- Most of the human published studies:
 - Dietary fiber
 - Fermentation not accepted as physiological benefit in new FDA fiber definition; fermentation is accepted in Canada
 - Prebiotics
 - Oligosaccharides, inulin, FOS, GOS, PHGG, acacia gum,
 - Probiotics
 - Fermented foods, yogurt, sauerkraut, kefir, sourdough



Dietary components altered by the gut bacteria

- Fermentable carbohydrates
- Proteins
- Vitamin synthesis
- Bile acids
- Phytochemicals/polyphenols
 - Phenolic acids, flavonoids, stilbenes, lignans, secoiridoids
- Rowland et al (2017) *Eur J Nutr* (09/04/17 online)





Prebiotic: a substance that is selectively utilized by host microorganisms conferring a health benefit



"Prebiotics are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and / or activity of one or a limited number of bacteria in the colon and thus improve host health"

- •Neither hydrolysed nor absorbed in the upper part of the GI tract
- •Selective substrate for one or a limited number of beneficial bacteria
- •Able to alter the colonic flora in favour of a healthier composition



Prebiotic dietary fiber sources

- Beta-glucan
- FOS, oligofructose, and inulin
- GOS
- Isomaltooligosaccharides
- Guar gum and PHGG
- Lactulose
- Resistant starch and maltodextrin
- Xylooligosaccharides and arabinooligosaccharides
 - Carlson J, et al. Curr Dev Nut 2018:2:nzy005.



DF & gut microbiota: review and meta-analysis

- 64 studies, 2009 participants
- DF resulted in higher abundance of Bifidobacterium and lactobacillus as well as fecal butyrate concentration compared to placebo
- Fructans and GOS led to greater abundance of both Bifidobacterium and lactobacillus compared to control
- No differences in effect were found between fiber intervention and comparators for alpha diversity, abundances of other pre-specified bacteria, or other SCFA concentration So et al. Am J Clin Nutr 2018;107:965-983.



PHGG, constipation, gut dysbiosis

- Added PHGG to diets of children with autism who presented with constipation.
- Decreased concentrations of serum interleukin 1beta and tumor necrosis factor-alpha.
- Also improved constipation symptoms
- Concluded the PHGG can improve constipation and gut dysbiosis symptoms, which in turn helped attenuate the level of serum inflammation cytokines and behavioral irritability

- Inoue et al. J Clin Biochem Nutr doi: 10.3164/jcbn.18-105.



Role of guar fiber in digestive health and function

- Summarized the clinically observed effects of guar fiber on digestive health
- Guar fiber normalized both constipation and diarrheal conditions
- It is effective in alleviating symptoms associated with IBS
- Regular intake of 5 to 10 g/d is effective to treat most of the morbidities associated with digestive health
- May offer potential protection and promotion of digestive health both alone and when combined with probiotics as a synbiotic formula
 - Rao & Quartarone. *Nutrition* 2019;59:158-169.



- No prospective, cohort studies that link changes in microbiota with health outcomes
 - Faecal samples not collected in epidemiological studies
- Disagreement on how to quantitatively measure in human studies
- Prebiotic standard protocols needed

Long term restriction of FODMAPs may lead to a decrease in prebiotic intake

* Brownawell AM, Caers W, Gibson GR, Kendall CW, Lewis KO, Ringel Y, Slavin JL. J Nutr 2012; 14(5): 962 - 974



FODMAPs

Acronym that stands for

Fermentable Oligo-, Di-, and Monosaccharides, And Polyols (FODMAP)

Term coined in 2005 by Australian researchers who theorize that foods containing these carbohydrates worsen symptoms of digestive disorders: Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD)

* Gibson PR, Shepherd SJ. Aliment Pharmacol Ther 2005; 21: 1399 - 1409



FODMAPs

- Concerns with the FODMAP concept
 - Recommendations based on clinical observations; few research trials
 - Grouping of all FODMAPs together, although perhaps easier for the patient, ignores physiological differences among FODMAPs
 - No regulatory guidance or official databases for FODMAP content
 - Low FODMAP diet is a low fiber diet
 - PHGG is a low FODMAP fiber



All dis-ease begins in the gut

> "LET FOOD BE THY MEDICINE

AND MEDICINE BE THY FOOD"

Microbiome Revolution

➤Gut Microbes Associated with Obesity

>12 Unrelated obese subjects on fat or carbohydrate restricted diet

>Monitored for one year

>Increase in Bacteroidetes correlates with change in weight





Diet may change gut microbial profiles in humans

Evidence From:

Observational studies

- Globally distinct populations
- Long-term food pattern consumption- Enterotypes



Short-term dietary interventions

- Low- versus high-fiber diets
- Animal versus plant food sources
- Macronutrient ratios

Arora and Backhed, J. Int. Med., 280:339, 2016



What microbes do in the body

- Produce additional energy otherwise inaccessible to the host
 - short chain fatty acids
- Produce vitamins in colon
 - Biotin. Vitamin K
- Metabolize carcinogens
- Provide ability to harvest nutrients
 - Enhance calcium absorption
- Prevent colonization by pathogens
- Assist in the development of a mature immune system



- 1. Organisms living on and within food may be either friends or foes to the consumer.
- 2. The human microbiome may decrease in diversity due to exposure to antibiotics, the consumption of a high-fat and high-sugar diet and decreased consumption of dietary fiber
- 3. Decreased diversity can increase susceptibility to invasive foodborne pathogens such as *Clostridium, Staphylococcus aureus, Escherichia coli and Listeria monocytogenes*
- 4. These organisms have greater potential to colonize and outcompete the host-associated community during dysbiosis
- 5. Some bacteria that are normal constituents of the microbiome and are sold as probiotics may become pathogenic such as *Escherichia coli*

Josephs-Spaulding et al. Appl Microbiol Biotechnol ePub April 22, 2016







Recent findings from American Gut Project

- Diversity of microbes in the gut is much more vast than originally thought
- Migration from a non-westernized nation to the US is associated with a loss of gut microbiome diversity
- Subjects who ate more than 30 types of plant foods weekly had more diversity than subjects who ate only 10 types of plant foods
- Diversity has not been linked to a health outcome



Conclusion - fiber

- Fiber intakes continue to be less than half recommended levels and new FDA rules for Nutrition Facts label will increase DV to 28 g/day
- It is no longer enough for an isolated fiber to analyze as fiber; it needs to show a physiological benefit to be fiber on the new Nutrition Facts panel
- Fermentation is not accepted as a health benefit for FDA
- FODMAPs may confuse consumers on the benefits of fiber
- Isolated fibers are the best solution to get fiber into the diet without calories; but trends toward whole foods and clean label present challenges for addition of isolated fibers to foods and drinks



Conclusions

- Microbiome research is an emerging area of science and there are many research opportunities available.
- The microbiome is integral to human physiology, maintenance of health and development of disease.
- There is a two-sided relationship between diet and the microbiome.
- Dietary fiber is known to alter gut health, including changes in the microbiota
- Prebiotics and are widely promoted, but not accepted by regulatory agencies
- Many developing links between changes in the microbiota and health outcomes, but no accepted "healthy" microbiota