The Role of Gut Health in the GLP-1 ERA

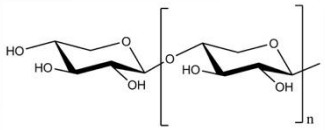
Mike Weiser, Ph.D.
VP R&D
AIDP

Topic Overview

How Gut Health Supplements and Functional F&B Can Support GLP-1 Receptor Agonist (RA) Consumers

Link Between GI System and GLP-1 RA Side Effects

Gut Microbiome and GLP-1 RA Effectiveness



Prebiotics and GLP-1

Functional Prebiotic GLP-1 Companion Ingredients

GLP-1 Receptor Agonists (RA) Are Gaining Popularity

$126B

Size of the global weight-loss medicine market by **2029**
Growing at an annual rate of **30%**
(According to UBS and Morgan Stanley Research)

300%

Growth GLP-1 drug prescriptions in the US alone between 2020 and 2023
(According to Barclays Research)

24M

Number of Americans projected to be taking GLP-1 drugs in **2035**
(Morgan Stanley research)

Ways That Gut-Health Supplements and Functional F&B Can Support

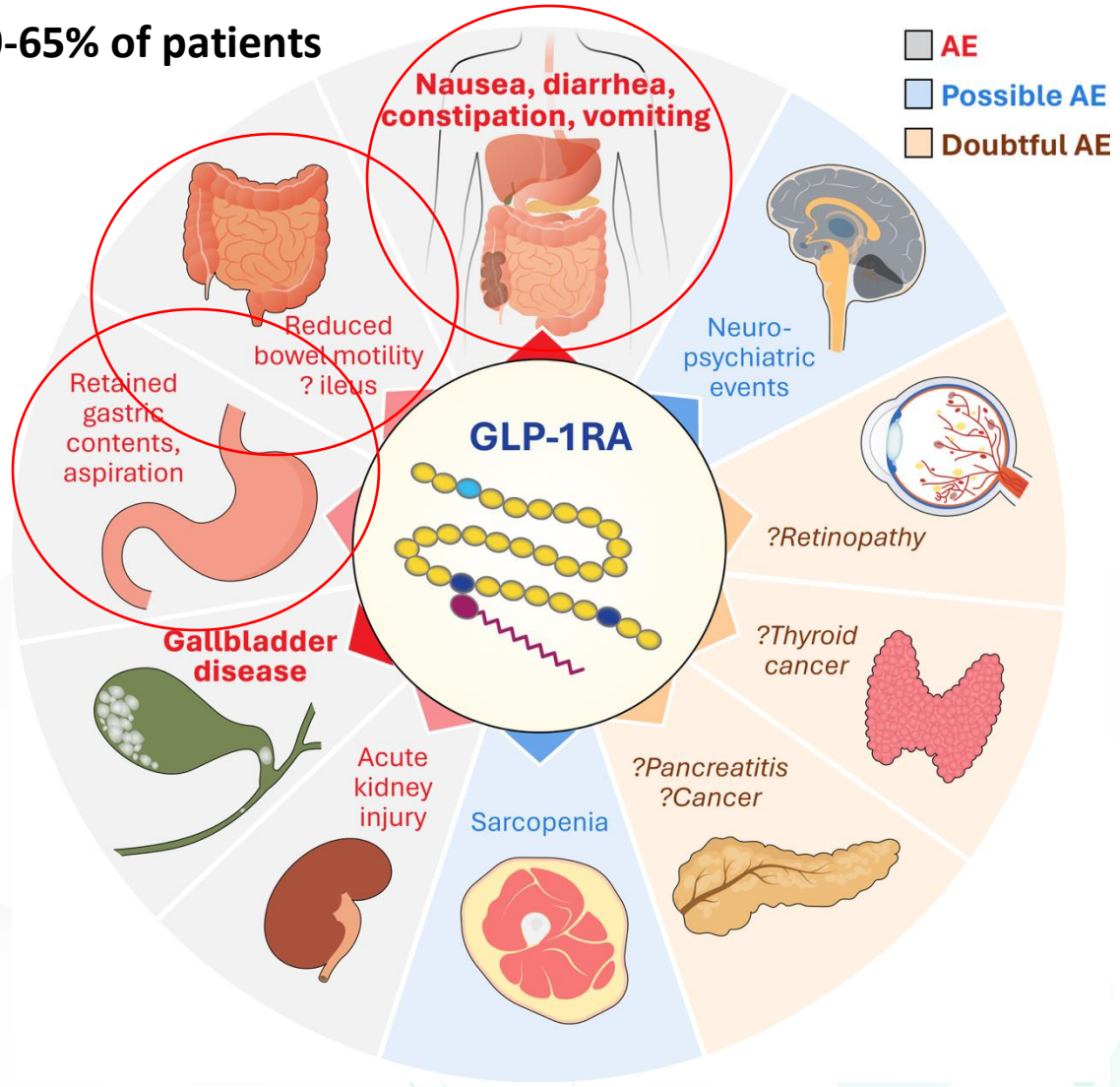
Companion products addressing side effects in a non-drug like way (normal structure function)

Supporting an ideal gut microbiome make-up which may impact the effectiveness of GLP-1 RAs

Maintenance of healthy metabolism and weight (especially for those coming off or cycling)

The GI System Is Central To GLP-1 RA Side Effects

40-65% of patients



Nausea and Heartburn

- GLP-1 drugs delay gastric emptying
- This leads to bloating, distension, heartburn and nausea sensation
- GLP-1 RA actions in the NTS (brainstem) can stimulate nausea feeling

Constipation

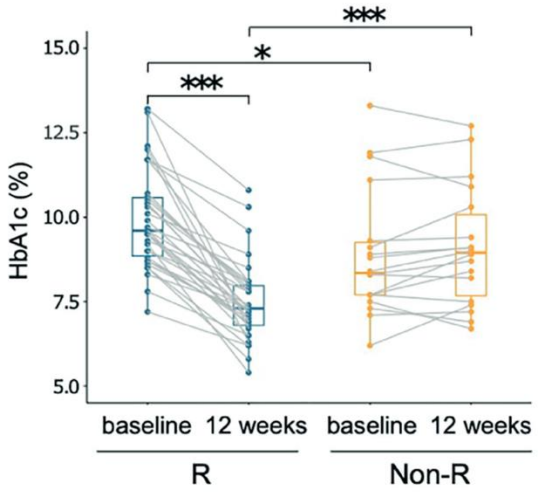
- GLP-1 receptor activation in the enteric nervous system reduces peristalsis and motility
- GLP-1 receptor activation in the brainstem modulates vagal output to decrease motility
- Slower transit time can increase constipation

Drucker, D. J. Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity. *Diabetes Care* 47, 1873–1888 (2024)
Nauck MA & Meier JJ. *Gastrointestinal effects of GLP-1 receptor agonists: clinical relevance and mechanisms*. Gut. (2019)

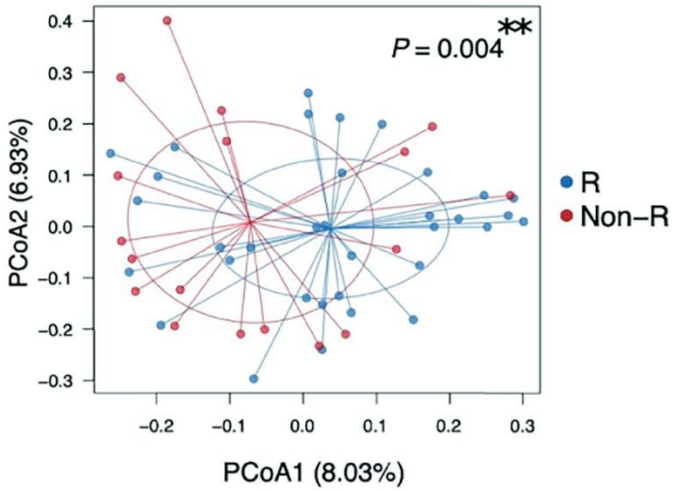
The Gut Microbiome is Key For GLP-1 RA Effectiveness

Recent human studies suggest that baseline microbiome profiles can predict how a patient will respond to GLP-1 RA therapy in terms of glycemic improvement or weight loss

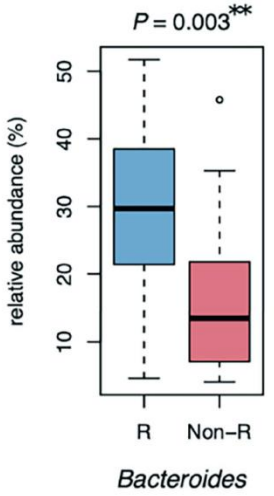
Non-Responders Defined as T2D Patients Without HbA1c Response



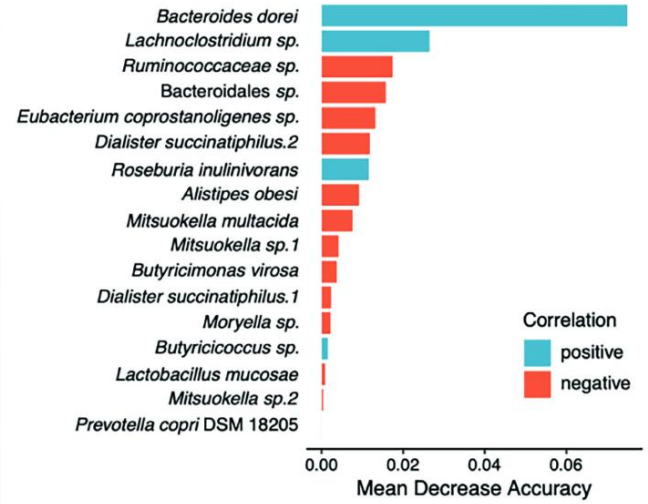
Beta Diversity is Different Between Responders and Non-Responders



Increases in Bacteroides in Responders



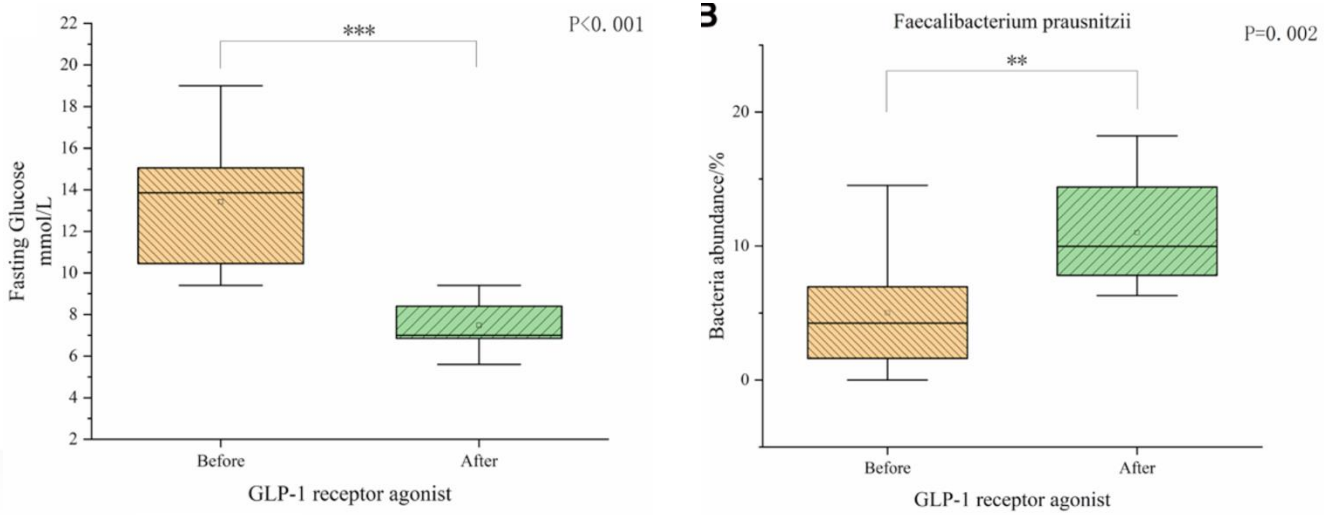
Certain Species Correlated with Effectiveness



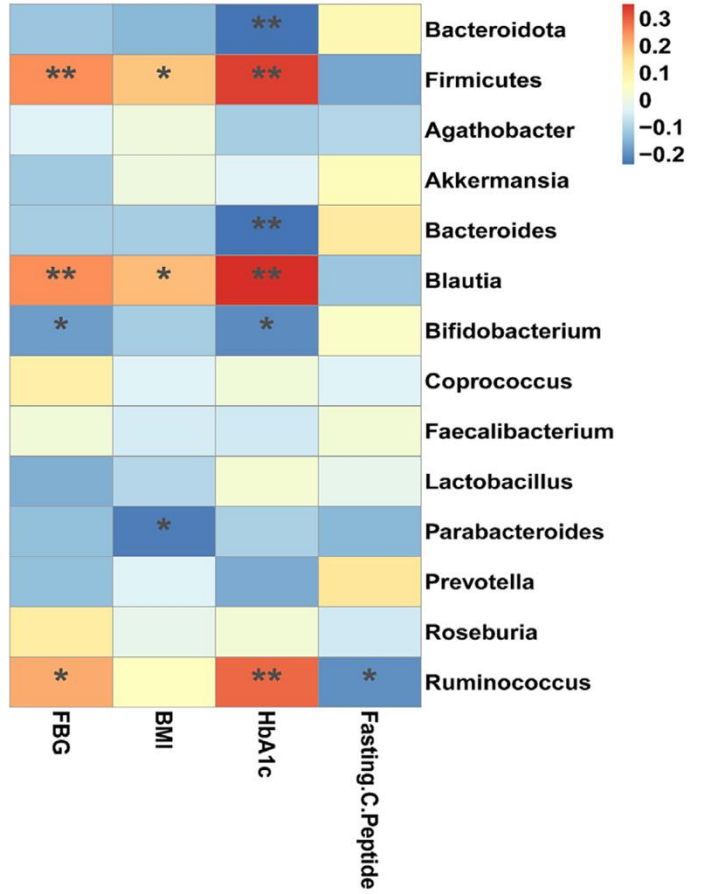
Tsai, C.-Y. et al. Gut Microbial Signatures for Glycemic Responses of GLP-1 Receptor Agonists in Type 2 Diabetic Patients: A Pilot Study. Front. Endocrinol. 12, 814770 (2022)

The Gut Microbiome is Key For GLP-1 RA Effectiveness

The emerging research points to the microbiome as a potential biomarker and mediator of GLP-1 RA treatment success



GLP-1 RA treatment in type 2 diabetics increased the abundance of *Faecalibacterium prausnitzii* after one week and was inversely corelated with fasting glucose level



GLP-1 RA altered the composition of the intestinal flora of newly diagnosed T2DM patients

The effect on HbA1c was correlated to several different groups of microbiota including Bifidobacteria

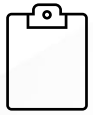
(1) Liang, L. *et al.* GLP-1 receptor agonists modulate blood glucose levels in T2DM by affecting Faecalibacterium prausnitzii abundance in the intestine. *Medicine* **102**, e34978 (2023)
(2) Liang, L. *et al.* Correlation between intestinal flora and GLP-1 receptor agonist dulaglutide in type 2 diabetes mellitus treatment—A preliminary longitudinal study. *iScience* **27**, 109784 (2024)

Maintenance of Healthy Metabolism and Body Weight

Can be difficult after-GLP-1 drug therapy

Research Study: Among ~8,000 U.S. users of Semaglutide (Ozempic®) or Tirzepatide (Zepbound®), only 32% remained on therapy at 1 year, a figure that drops to ~15% by 2 years

Clinical Trial: When Semaglutide was stopped after ~68 weeks, roughly two-thirds of the weight lost was regained within 1 year



Consumer Survey: 66% percent regained a portion of their weight, 23% maintained their weight loss, and only 11% continued to lose weight after discontinuing taking a GLP-1

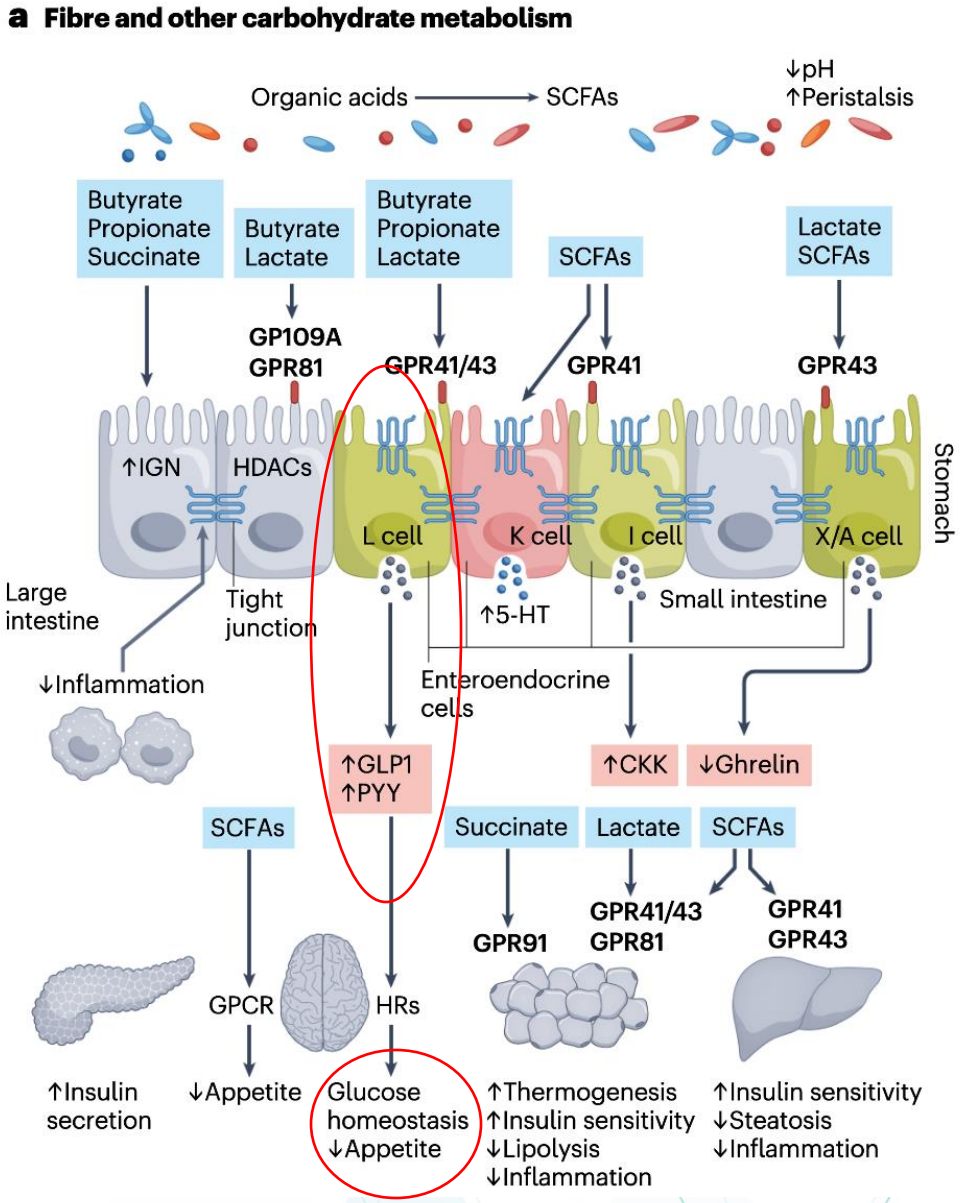
Takeaway for the Functional Supplement, Food & Beverage Market:
There is white space for complimentary solutions here to support a healthy metabolism and healthy weight maintenance…like gut health supporting prebiotics…

Gasoyan, H. et al. Changes in weight and glycemic control following obesity treatment with semaglutide or tirzepatide by discontinuation status. Obesity (2025)

Jensen, S. B. K. *et al.* Healthy weight loss maintenance with exercise, GLP-1 receptor agonist, or both combined followed by one year without treatment: a post-treatment analysis of a randomised placebo-controlled trial. *eClinicalMedicine* **69**, 102475 (2024)

Omada Survey November 2024: "GLP-1 Discontinuation: Real-World Perspectives on a Complex Journey"

Prebiotics Via Metabolites Like SCFAs Help Stimulate GLP-1



Review Article | Published: 04 June 2025

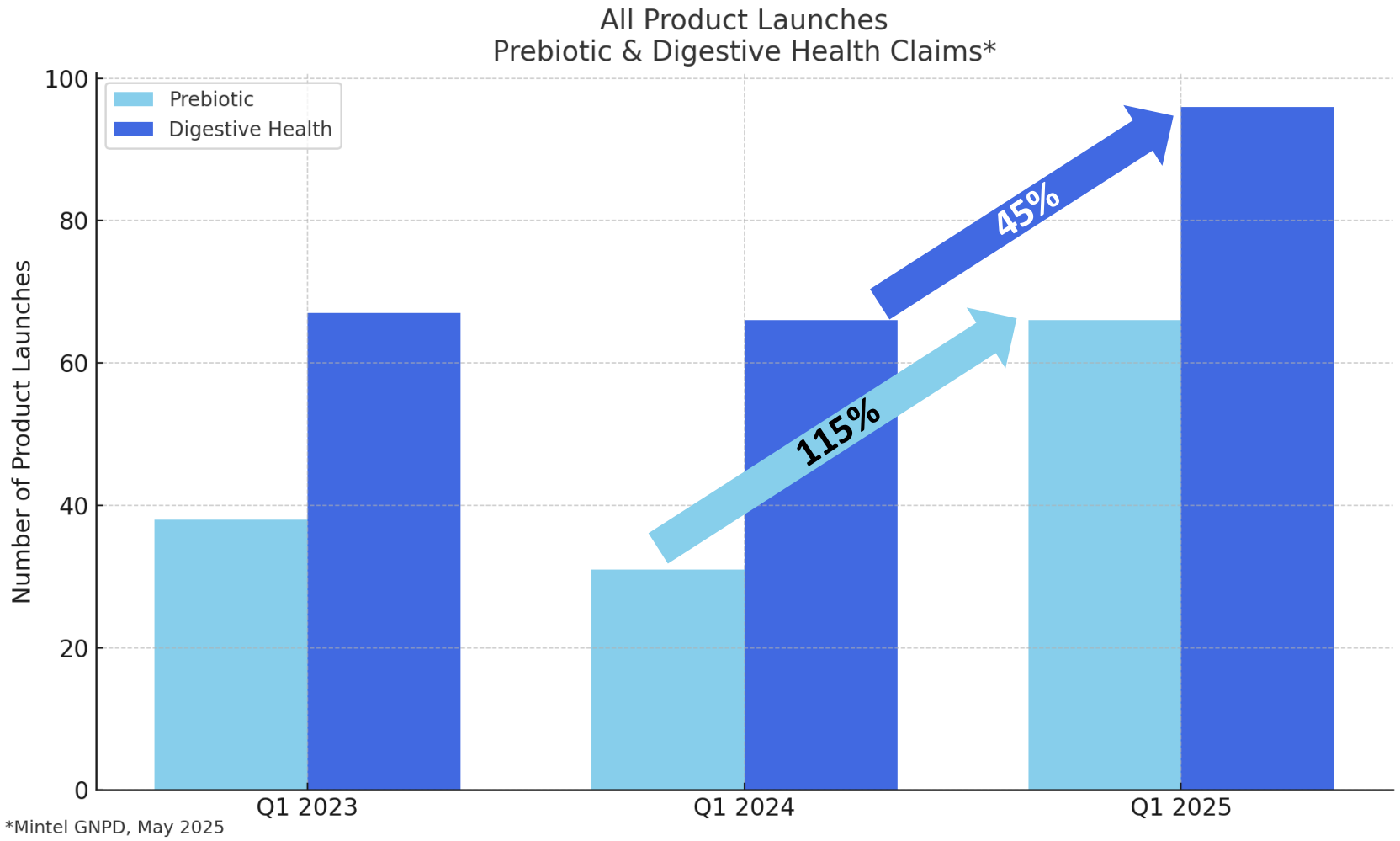
The gut microbiome connects nutrition and human health

Yolanda Sanz, John F. Cryan, Mélanie Deschasaux-Tanguy, Eran Elinav, Rebekka Lambrecht & Patrick Veiga

Nature Reviews Gastroenterology & Hepatology (2025) | Cite this article

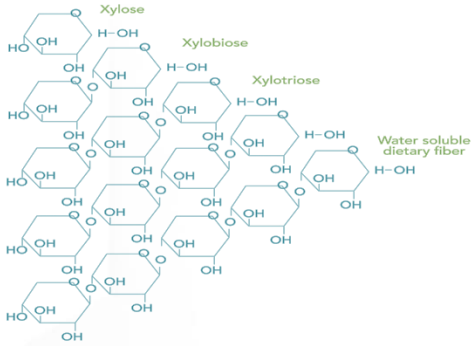
- Prebiotics increase short chain fatty acids
- These fatty acids can act via GPR41/43 on enteroendocrine L cells to increase GLP-1 and PYY secretion
- These hormones work to decrease appetite and improve homeostasis of blood glucose
- Research is emerging on the benefit of prebiotics for supporting metabolism and a healthy weight

Launches With Prebiotic Claims Are Exploding



*Mintel GNPD, May 2025

Functional Prebiotic GLP-1 Companion Ingredient Examples



PreticX
Optimize Your Flora

Plant Based Xylo-Oligosaccharides

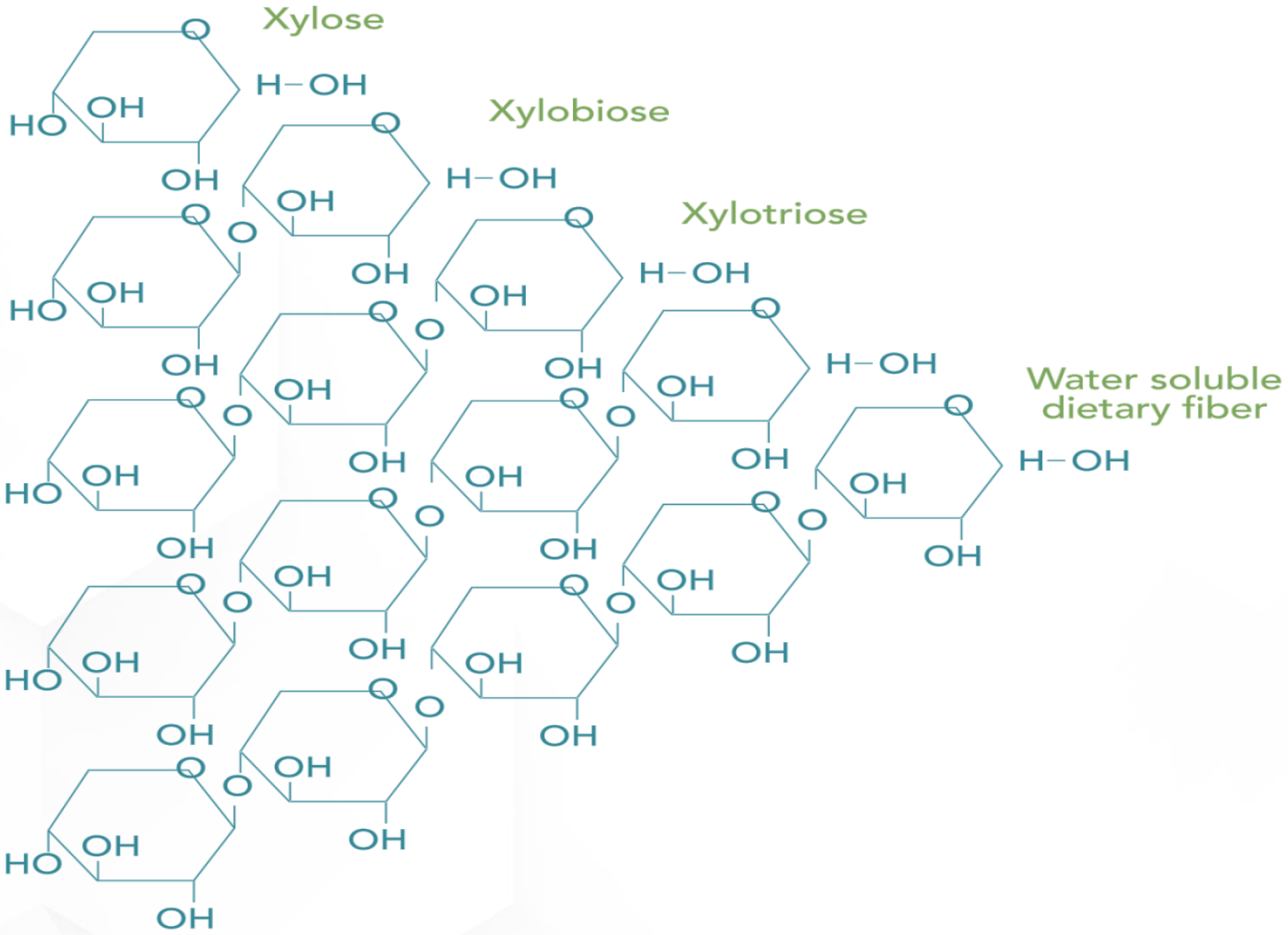
ACTAZIN®

Freeze-Dried Whole Green Kiwi Fruit

GutGard®

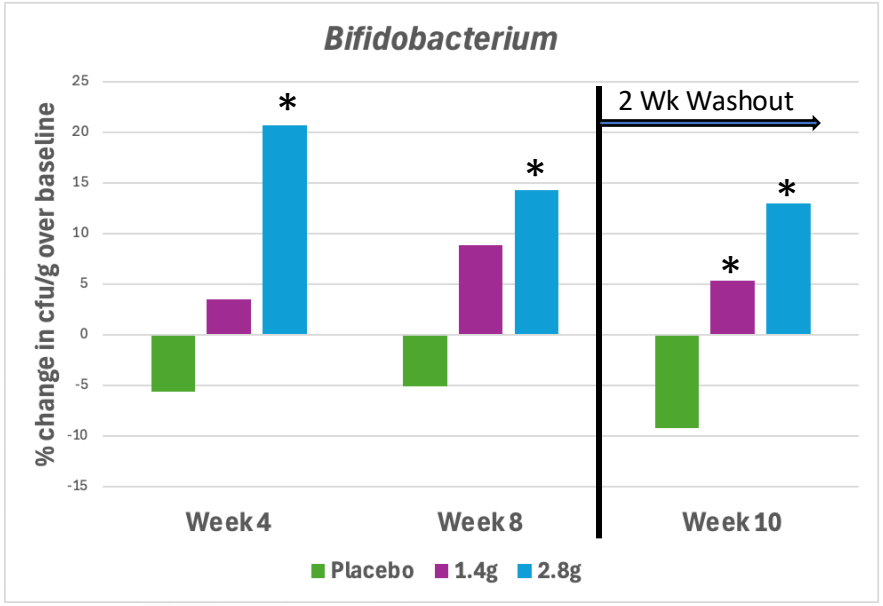
Polyphenol Rich Licorice Extract

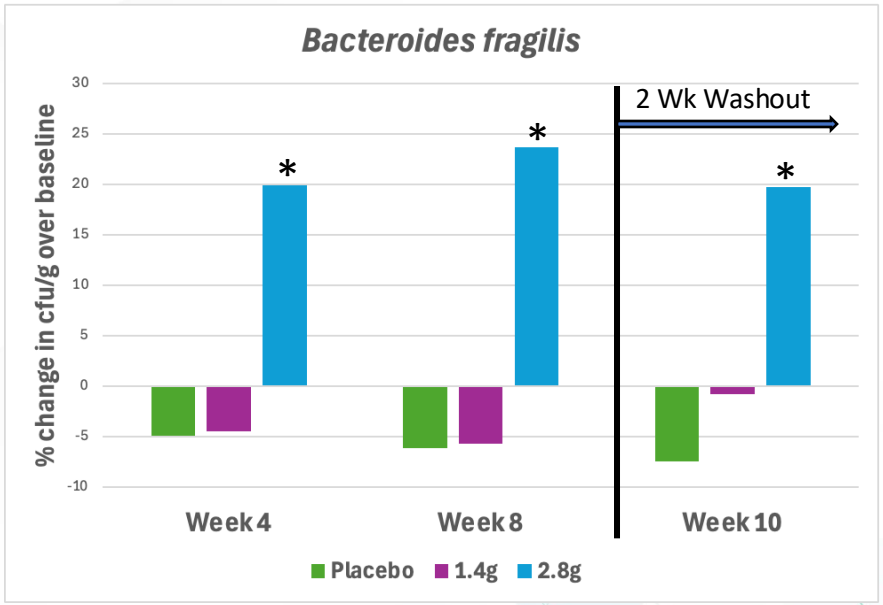
Xylo-Oligosaccharides



- Oligosaccharide of xylose molecules with β-1, 4 glycosidic bond
- Manufactured via enzymatic hydrolysis of xylan from corn cob
- Non-digestible prebiotic fiber
- Remodels gut microflora composition, improves *Firmicutes:Bacteroidetes* ratio
- Promotes *Akkermansia*
- Improves cardiometabolic measures

Xylo-Oligosaccharides Increase GLP-1-Relevant Microbes





Design

- Double-blind, randomized, placebo-controlled
- 32 healthy adult participants
- 1.4g or 2.8g of PreticX® per day, or placebo
- 8-week supplementation with 2-week washout

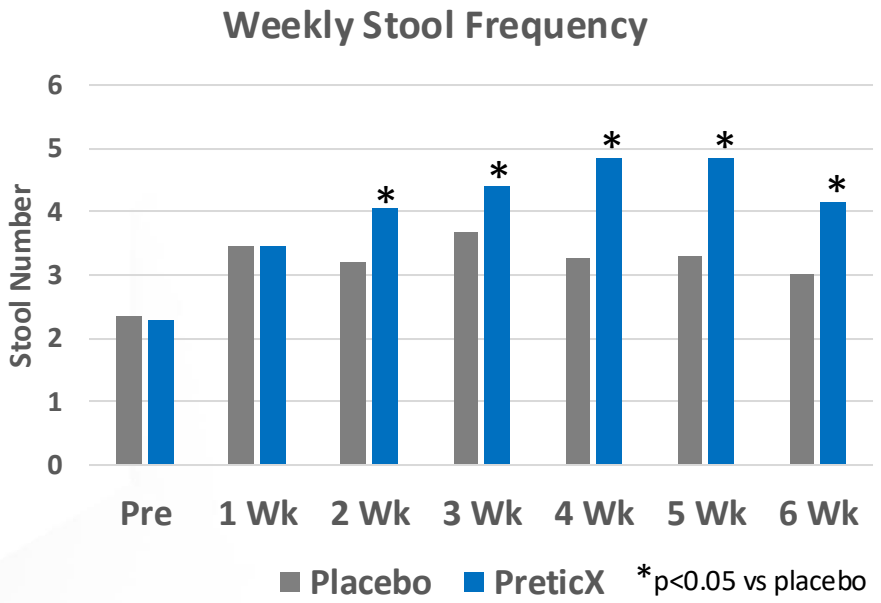
Results

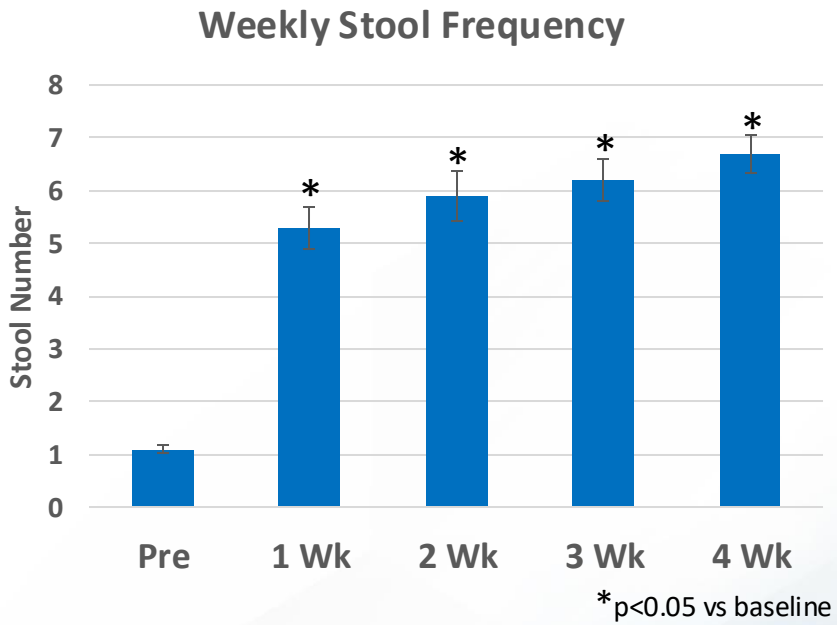
- Increase in absolute ***Bifidobacterium*** from baseline was significantly greater for both doses at week 10 and the higher dose also at week 4 and week 8
- Increase in absolute ***Bacteroides fragilis*** from baseline was significantly greater for the 2.8g per day dose at all time points
- Significant increase in relative ***Akkermansia*** for the 2.8g dose compared to placebo (p=0.041)

*$p<0.05$ vs placebo

Finegold, S. M. *et al.* Xylooligosaccharide increases bifidobacteria but not lactobacilli in human gut microbiota. *Food Funct.* **5**, 436–445 (2014)

Xylo-Oligosaccharides Promote Gut Motility





Design
- Double-blind, randomized, placebo-controlled
- 700mg of PreticX® per day, or placebo for 6 weeks
- 56 young women with constipation (mean age 22)

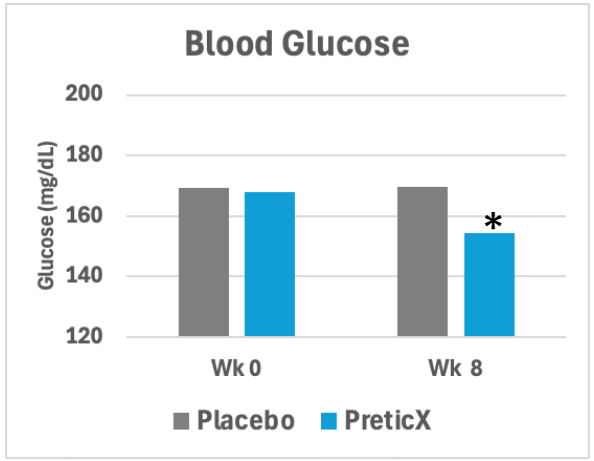
Results
- Beginning at week 2 the PreticX® group had significantly more weekly stools compared to placebo

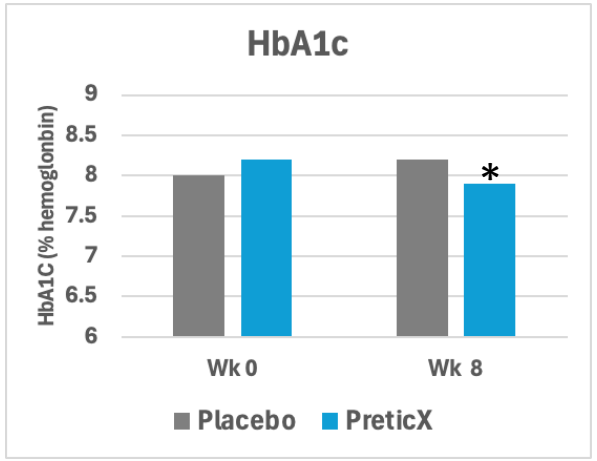
Design
- Open label intervention
- 3g of PreticX® per day for 4 weeks
- 27 pregnant women with constipation

Results
- PreticX® significantly increased the number of weekly stools from one-per-week to nearly seven-per-week

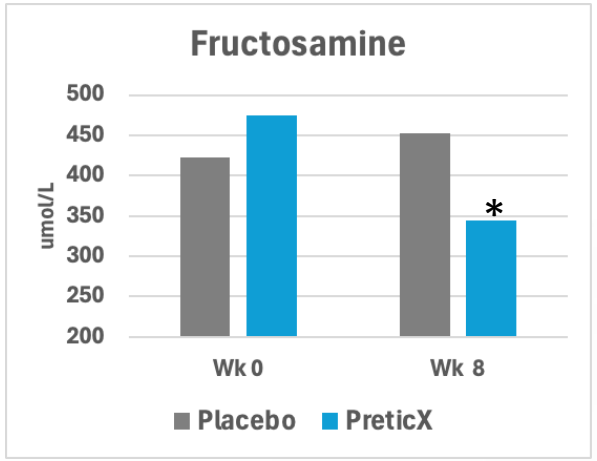
1. Jeon, J. H., Kyung, M., Jung, S., Jo, S. & Chang, M.-J. Effect of xylooligosaccharide-sugar mixture on defecation frequency and symptoms in young women with constipation: a randomized, double-blind, placebo-controlled trial. J. Nutr. Heal. 48, 19–29 (2015)
2. Tateyama, Ichiro, et al. "Effect of xylooligosaccharide intake on severe constipation in pregnant women." *Journal of nutritional science and vitaminology* 51.6 (2005): 445-448

Xylo-Oligosaccharides Impact Glucose Metabolism

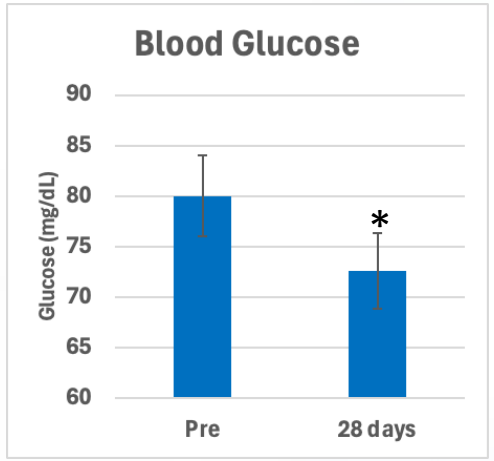




*p<0.05 change from baseline is significantly different vs placebo



Measure of short-term (2-3wk) BG levels



*p<0.05 vs baseline

Design

- Double-blind, randomized, placebo-controlled
- 4g of PreticX® per day, or placebo for 8 weeks
- 26 adults with type-2 diabetes (HbA1c between 7 and 10%)

Results

- PreticX® significantly lowered:
  Glucose metabolism measures: • Fasting blood glucose • HbA1c • Fructosamine
  Lipid metabolism measures: • Total cholesterol • LDL cholesterol • apolipoprotein B

In a separate study in 14 healthy women 2.8g/day of PreticX for 28 days decreased fasting blood glucose, cholesterol, and triglyceride concentrations

PreticX® Optimize Your Flora

1. SHEU, W. H.-H., LEE, I.-T., CHEN, W. & CHAN, Y.-C. Effects of Xylooligosaccharides in Type 2 Diabetes Mellitus. *J. Nutr. Sci. Vitaminol.* **54**, 396 (2008)
2. Na, Mi-Hee, and Woo-Kyoung Kim. "Effects of xylooligosaccharide intake on fecal Bifidobacteria, lactic acid and lipid metabolism in Korean young women." Journal of Nutrition and Health 40.2 (2007): 154-161.

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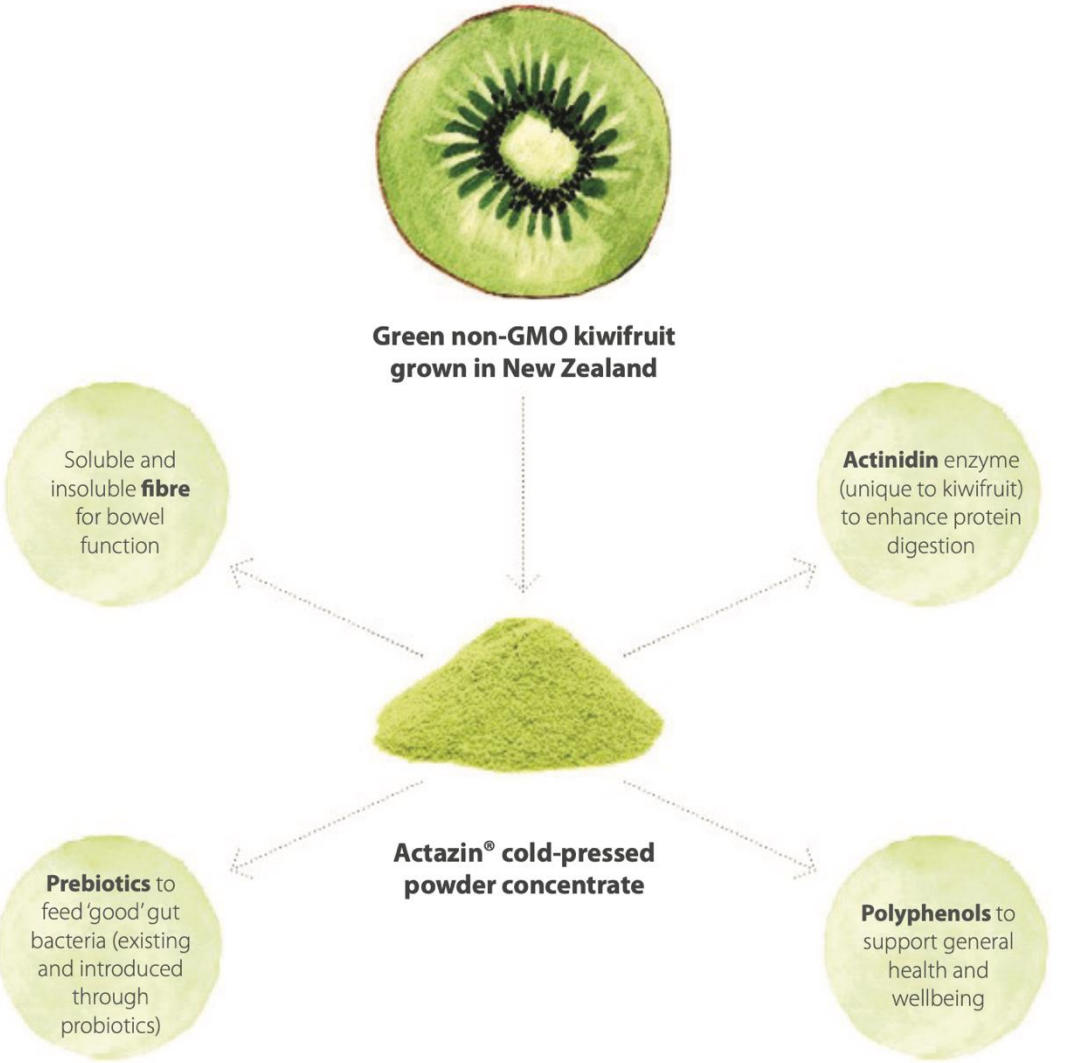
Freeze-Dried Whole Green Kiwi Fruit

- Kiwi Fruit fiber swelling capacity is 1.5X psyllium and 6X apple fiber
- Rich in polyphenols and prebiotic polysaccharides (xyloglucan and pectin predominantly)
- Fermentable by colonic microbiota
- Increases colonic microbial biomass and fecal bulking
- Supports mucin production
- EFSA Health Claim: “Consumption of 2 whole green kiwifruit (*Actinidia deliciosa* var. Hayward) contributes to the maintenance of normal defecation”



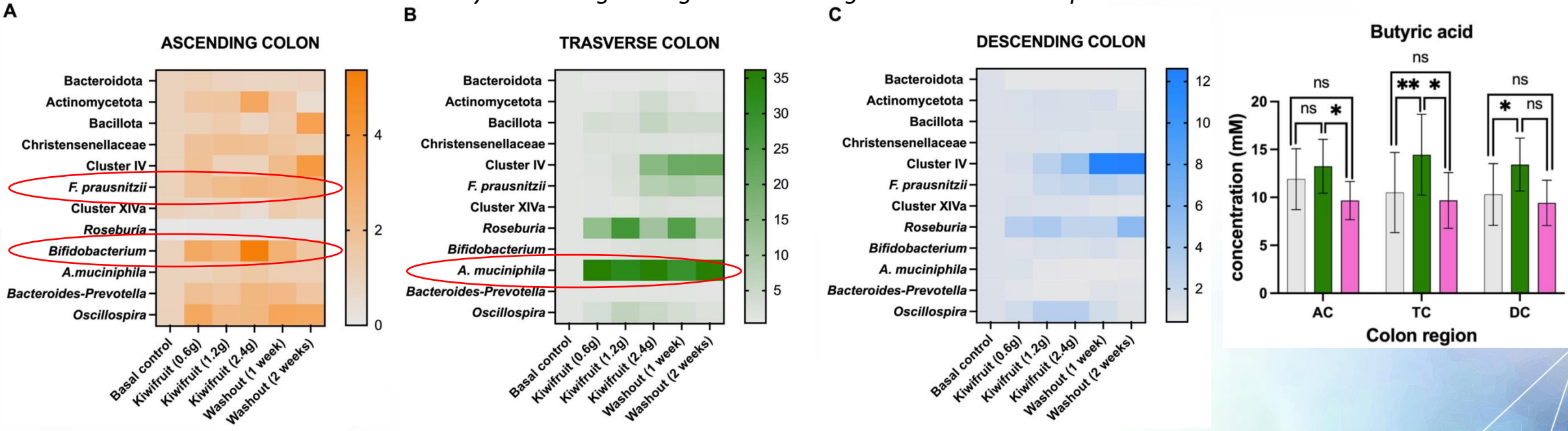
ACTAZIN®

Freeze-Dried Whole Green Kiwi Fruit

Actazin® promotes the growth of Akkermansia, Bifidobacteria, and Faecalibacteria and increases butyrate

Simulator of the Human Intestinal Microbial Ecosystem (SHIME®)

Dynamic long-term gut model using human donor samples



Goya-Jorge, E. *et al.* Butyrogenic, bifidogenic and slight anti-inflammatory effects of a green kiwifruit powder (Kiwi FFG®) in a human gastrointestinal model simulating mild constipation. *Food Res. Int.* **173**, 113348 (2023)

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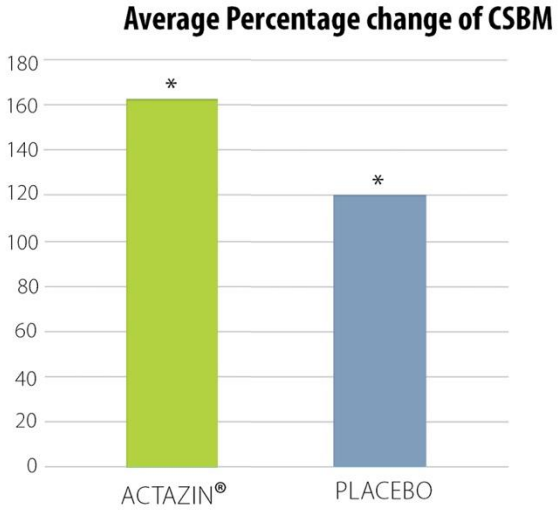
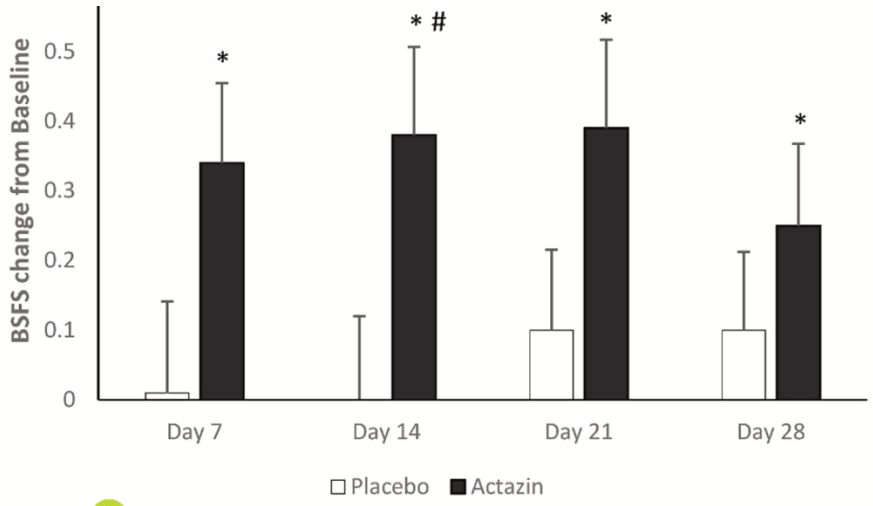
Freeze-Dried Whole Green Kiwi Fruit





Actazin® significantly improves gut motility and stool quality in a placebo-controlled DB RCT

Design
- Parallel, blinded, placebo-controlled
- Multi-center (four)

Population
- 18–60-year-old healthy adults with occasional constipation
- Less than 30g of daily fiber intake

Intervention
- 600mg Actazin or placebo (cellulose)

ACTAZIN®

Graham, E. et al. Actazin® green kiwifruit powder consumption at 600 mg per day for 28 days improves stool form and relieves occasional constipation in healthy individuals: A randomized controlled trial. Bioact. Carbohydr. Diet. Fibre 32, 100436 (2024)

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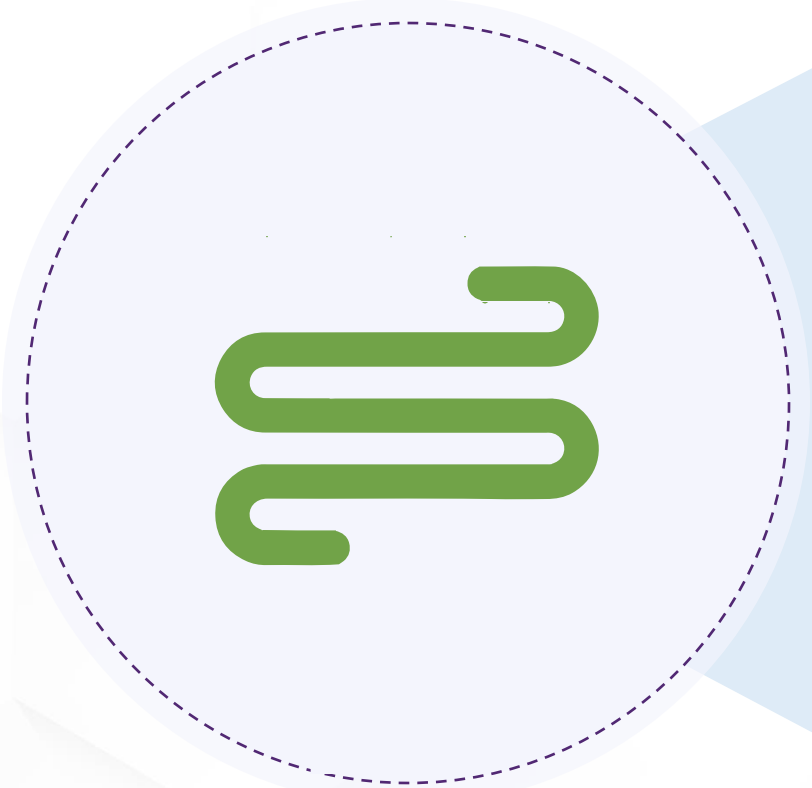
Flavonoid Rich Licorice Extract

Flavonoids are prebiotic and support digestive health

Flavonoids are a class of polyphenolic secondary metabolites found in plants widely researched to benefit digestive health



01 Flavonoids and flavonoid metabolites can **shape gut microbiota** by **inhibiting** the **growth of** various **pathogens** and **increasing beneficial genera**

02 Flavonoids **inhibit gut inflammation**

03 Flavonoids are studied to **improve gut immunity**

GutGard®

Pei, R., Liu, X. & Bolling, B. Flavonoids and gut health. Curr. Opin. Biotechnol. 61, 153–159 (2020)

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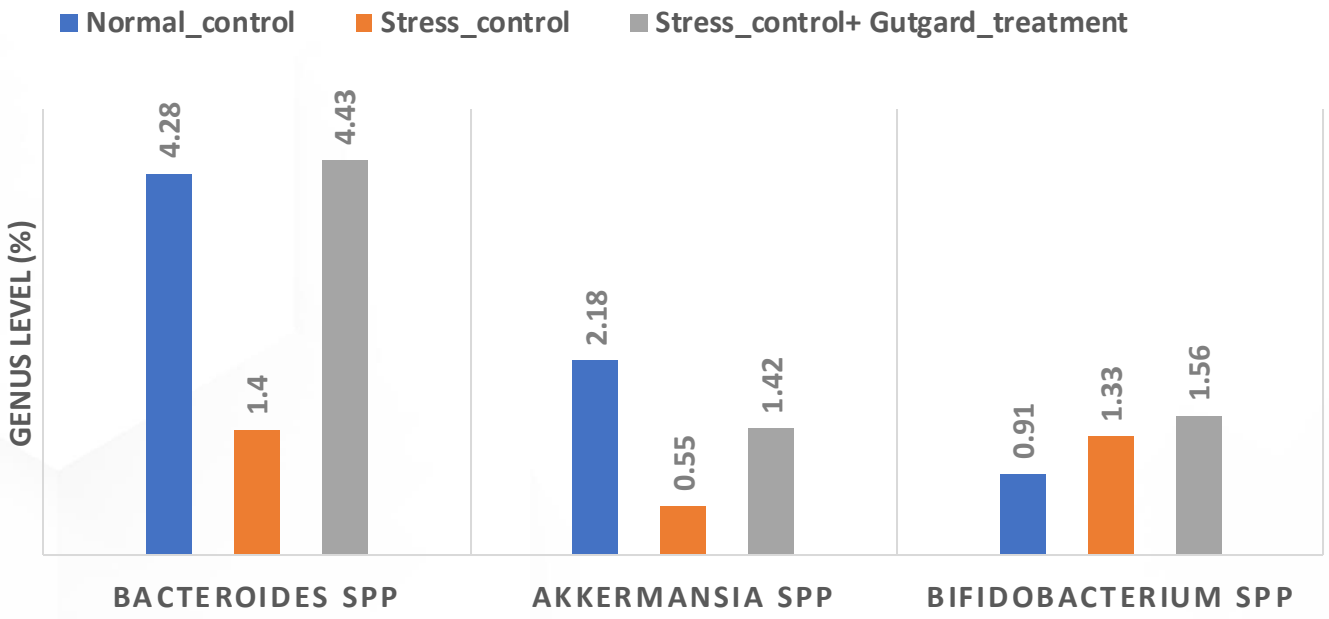
Flavonoid Rich Licorice Extract

GutGard® significantly improves stress-induced gut dysbiosis



- Restraint stress induced gut dysbiosis
- Normal control, stress control, and GutGard®-treated groups.
- 120-minute daily restraint stress for 10 days.
- GutGard® administered for 7 days before and 10 days during restraint stress.

GutGard® at 150 mg HED **promotes** the growth of beneficial bacteria linked to GLP-1 RA effectiveness (*Bacteroides spp, Bifidobacterium spp)* and healthy metabolism (*Akkermansia spp)*

Some of these are butyrate producers which may be able to help stimulate GLP-1 production by enteroendocrine L cells

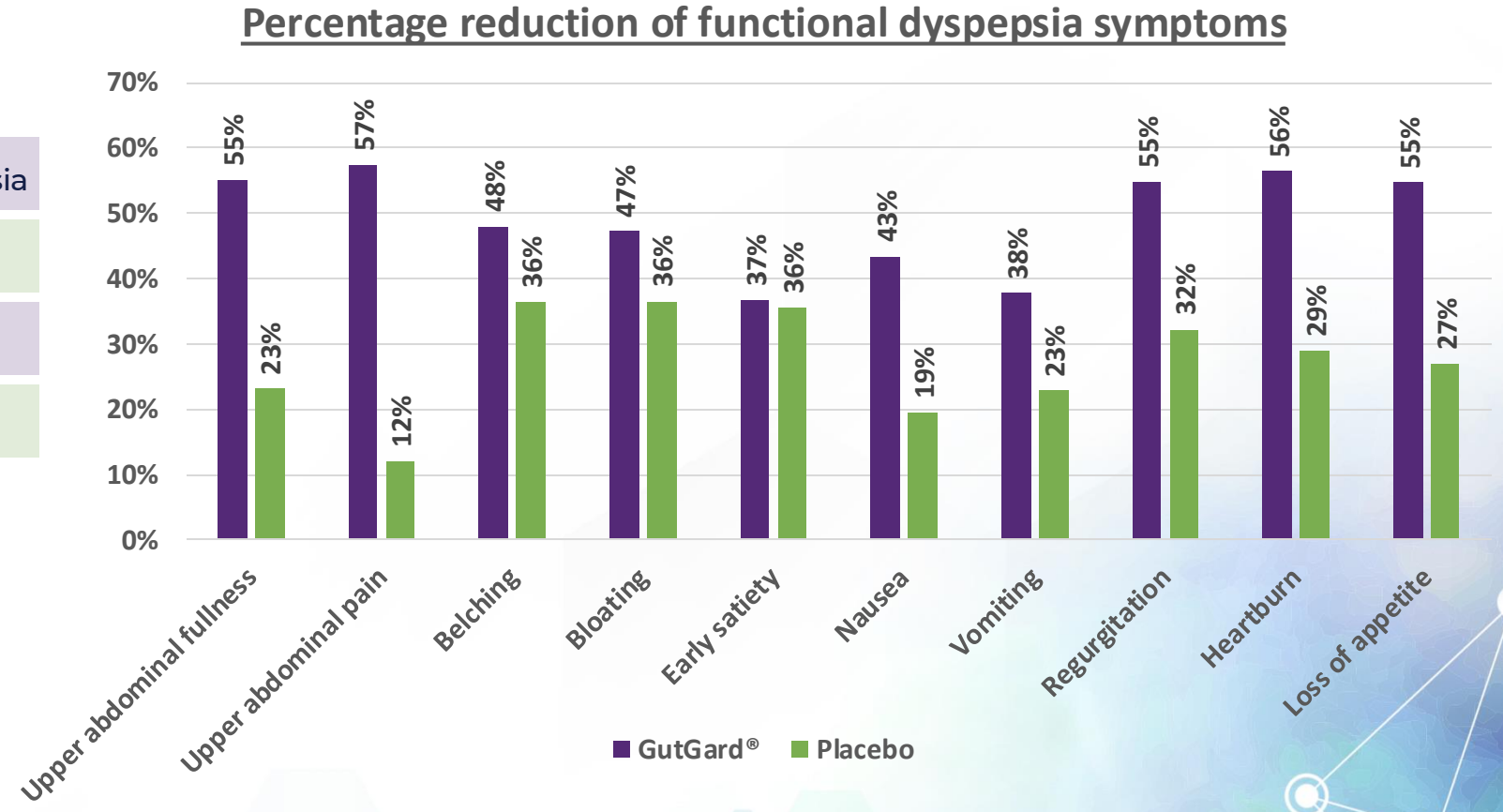
GutGard®

Flavonoid Rich Licorice Extract

GutGard® significantly lowers symptoms of functional dyspepsia in a placebo-controlled DB RCT

Condition	Subjects with Functional dyspepsia
Dose	75 mg twice a day after food
Participants	50 subjects (Age: 18-65 years)
Duration	30 days

Many of these symptoms overlap with GLP-1 RA side effects



GutGard

Raveendra et al. Evidence-Based Complementary and Alternative Medicine 2012, Article ID 216970, 9 pages, 2012.

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Summary – Take Home Key Points

GLP-1 RAs have revolutionized the weight loss market, increasing the focus on supportive and complimentary supplements and functional foods and beverages

Gut health and the gut microbiome may have an important impact on GLP-1 RA efficacy (responders/non-responders), side-effects, and maintenance of a healthy weight

Prebiotic ingredients can supplement a healthy diet to support healthy gut motility, the gut microbial composition, and a healthy metabolism and body weight

PreticX Optimize Your Flora

ACTAZIN

GutGard

Thank You!

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www.linkedin.com/in/mike-weiser-phd/