

Clinical Findings on Synergies Between Select Prebiotics

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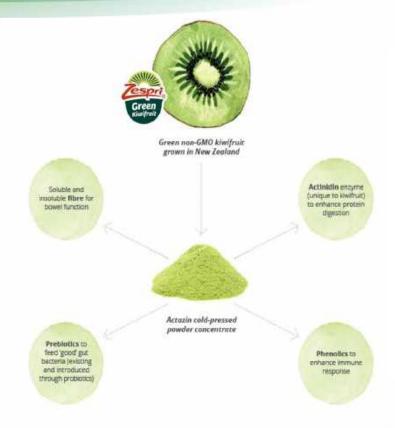


Business Confidential



Green Kiwifruit Powder for Digestive Regularity

- · Food-quality digestive health ingredient
- Derived from New Zealand green kiwifruit
- Developed using proprietary, pharmaceutical grade freeze-drying method
- Chemical-free and solvent-free production
- Actinidin enzyme for protein digestion
- Soluble + insoluble fiber for laxation
- Kiwifruit pectin for microbiome support
- Non-GMO, Kosher, Halal, Organic available



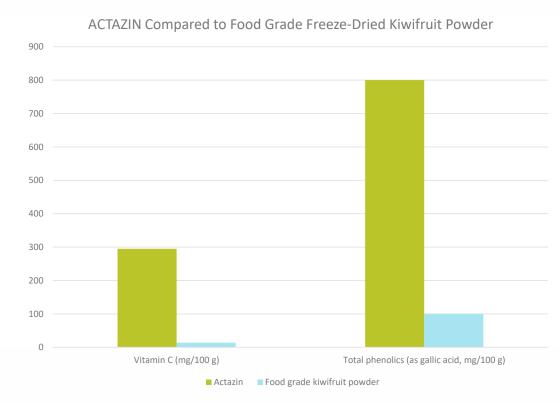




ACTAZIN vs Food Grade Freeze-Dried Kiwi

Actazin has 21 times more Vitamin C and 8 times more Phenolics than food grade kiwi powder.

Dietary fiber in food grade kiwi powder is hardly present and Actinidin cannot be detected.







Previous Clinical Results

Nearly 20% More Bowel Movements

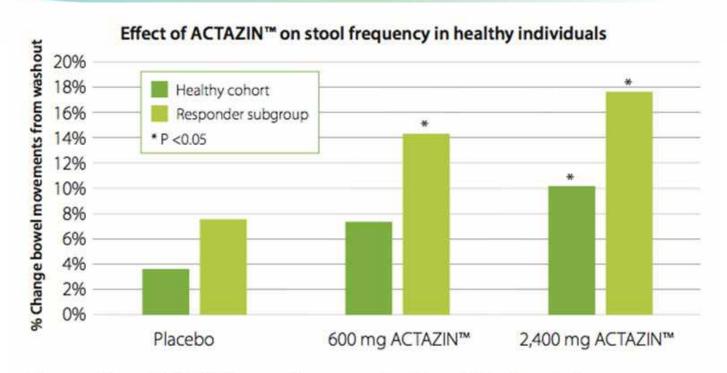


Figure 2: Effect of ACTAZIN™ on stool frequency in healthy individuals, as whole group and the subgroup responders.

Ansell et al. 2015. Nutrition Research, 35(5): 401-408



Mechanism of Action

- Increase mucus production in the gut
- 2. Improve gut transit & faecal bulking
- 3. Reduce excessive nitric oxide (NO) production

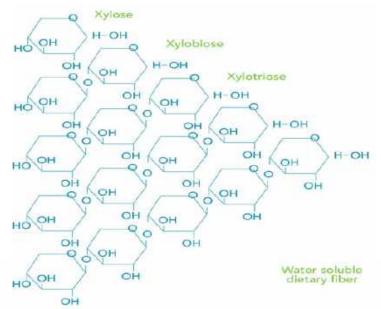
Physiological Function	Pathway	Biomarker
1. Mucus Production	mTOR signalling	Mucin 2
2. Gut Transit	GPR-41 (gastric emptying)	GLP 1
	GPR-43 (gut transit time)	PYY
	M3R (smooth muscle relaxation via acetylcholine)	PCK-a
3. Nitric Oxide (NO) Production	TNF-α signalling pathway	Nitric Oxide (NO)





Low Dose XOS Prebiotic for Bifidogenic Reconditioning



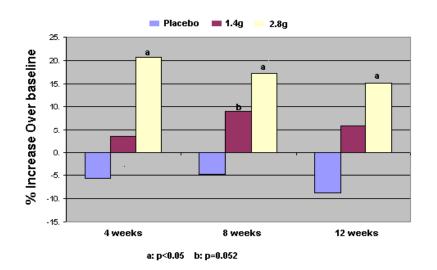


- Low-dose xylooligosaccharide (XOS) prebiotic
- Produced by patented manufacturing process via enzymatic hydrolysis of non-GMO corn cob
- · Selective **bifidogenic** activity at 1 gram per day
- . Optimizes gut flora
- · Supports metabolic health
- Backed by more than 12 published clinical trials
- Low water activity (<0.17)
- FDA GRAS, EFSA and Health Canada Approved with qualified health claims
- Kosher, Halal and Non-GMO Project Verified
- Organic available





Increases Bifidobacterial Dosing as low as 1g/day



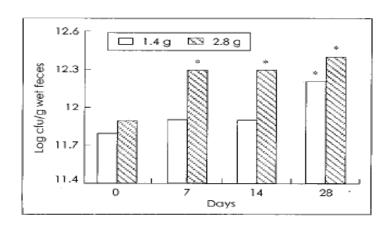


Figure1: PreticX increases Bifidobacterial as low as 1.4g/day

A: UCLA study (Dr. Li and Dr. Heber, et al Food Funct., 2014, 5, 436)

B: Korean study (韓國營養學會誌 40(2):154~161, 2007)



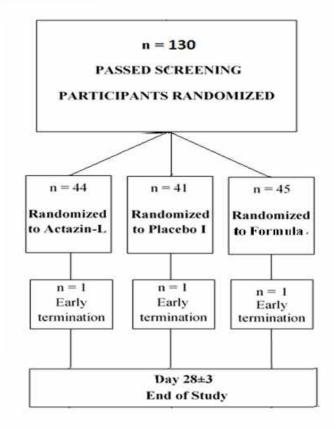


Can we have a synergistic product that benefits both Regularity and Microbiome?

Double-blind, Placebo-Controlled, Multicenter study of 2018-2020

- Hypothesis four weeks of daily consumption of Actazin® and Actazin +PreticX® would relief constipation in healthy participants who ordinarily had ≤ 3 CSBM per week
- **4 Centers** London Ontario; Toronto Ontario; Chicago IL; Boca Raton FL.
 - Actazin® 600 mg daily
 - Actazin® 600mg + PreticX® 1g
 - Placebo Cellulose

Compliance for all groups was >95%.





Inclusion Criteria

- 1. Males and females 18 to 60 years of age
- Body mass index (BMI) between 19 and 29.9 \pm 1 kg/m² at screening, inclusive
- 3. Self-reported \leq 3 CSBMs per week at screening and confirmed in the BHD during the run-in period for enrolment at baseline
- 4. People who were not regular consumers of high fiber diets, yoghurt, fermented foods such as kimchi, kombucha, sauerkraut, etc.
- 5. Fasting blood glucose $\leq 6.0 \text{ mmol/L}$ at screening
- 6. Agreed to refrain from the consumption high-fiber dietary supplements including Metamucil, Benefibre, and Phloe
- 7. Agreed to refrain from the consumption of fresh kiwifruit 2-weeks prior to and during the study
- 8. Agreed to maintain their habitual food and beverage intakes and life style
- 9. Had given voluntary, written, informed consent to participate in the study



Clinical Measurements

BSS – Bristol Stool Scores

A diagnostic scale which classifies stool form into 7 types, from hard to watery.

Important objective measure of constipation

CSBM – Complete Spontaneous Bowel Movements

Bowel movements occurring without medication or intervention and provide feeling of complete evacuation.

Changes in CSBM of only 1 per week are considered clinically significant.

Participant-assessed (subjective) scoring.

PAC-QoL, PAC-SYM and other Safety Parameters

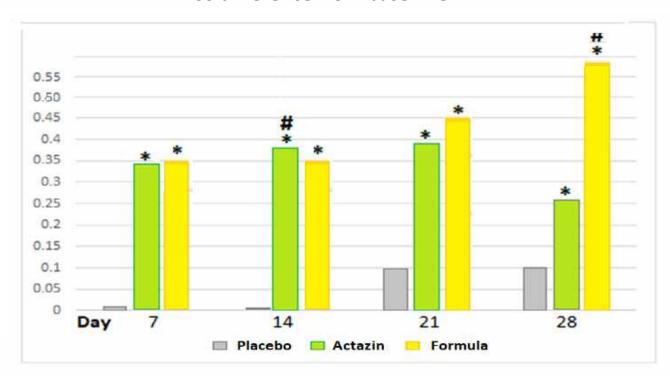
Alternative Bristol Stool Chart





Results: Actazin® and PreticX® Improve BSS Synergistically

BSS difference from base line



* P<0.05 as compared to the baseline. # p<0.05 as compared to the Placebo

Actazin® and **Formula** improved the normality of stool form of the participants through out the study



Topline Conclusions: Actazin® and Actazin®+PreticX® Formula

- Actazin® showed statistically significantly improved BSS over baseline and Placebo
- Actazin®+PreticX® Formula showed statistically significantly improved BSS over baseline and Placebo
- Actazin®+PreticX® Formula demonstrated synergistic effects









New Publication: Patients With COVID-19 DuringHospitalization Indicate Alterations in Gut Microbiota

Gastroenterology 2020;159:944-955

Table 1. Subject Characteristics

Variables	COVID-19 cases	Pneumonia controls	Healthy controls	
Number	15	6	15	
Male	7 (47)	4 (67)	9 (60)	
Median age, y (IQR)	55 (44, 67.5)	50 (44, 65)	48 (45, 48)	

Method:

- ➤ Shotgun metagenomic sequencing analyses of fecal samples
- Compare gut microbiome profiles in association with disease severity and changes in fecal shedding of SARS-CoV-2.

Study Results

- ➤ Patients with COVID-19 had significant alterations in fecal microbiomes compared with controls,
- There was an inverse correlation between abundance of Faecalibacterium prausnitzii (an anti-inflammatory bacterium) and disease severity

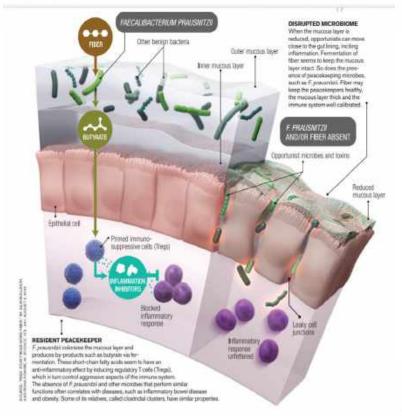
Bacteria taxa	Correlation coefficient Rho	<i>P</i> value
p Firmicutesic Clostridiajo	·····o	
Clostridiales f Ruminococcaceae g		
Faecalibacteriumjs Faecalibacterium_prausnitzii	0.87	.011
Do at a wall data alla		
p Bacteroidetesjc		
Bacteroidiajo Bacteroidalesjf		
Rikenellaceaejg Alistipesis Alistipes_onderdonkii	0.90	.005

Faecalibacterium prausnitzii (F. prau)

F. prau is a special bacterial species that resides in the gut, accounting for approx. 5% - 15% of the total gut microbiome.

F. prau has digestive health and wellness benefits:

- Readily ferments soluble fiber and polyphenolic compounds
- Increases butyrate production
- Reduced F. prau has been associated with a range of gastrointestinal disorders, such as IBS, IBD and chronic constipation.







Gold Kiwifruit – Immune Enhancing Benefits

Gold kiwi has been shown to enhance immune response via increased production of T-helper cells, IgG antibodies, and cytokine IL-5.

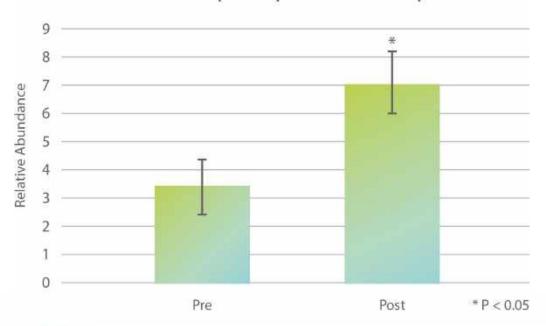
- Hunter, et al 2012 gold kiwi consumption led to overall reduction in incidence of cold and influenza-like illness ar reduction in symptoms in children 2-5 years.
- Skinner, et al 2012 gold kiwi consumption significantly reduced head congestion, sore throat symptoms and lipid peroxidation in older adults.





Published Clinical Results – 2-fold Increase in F. prau Abundance

Relative abundance of F.Prau in functionally constipated individuals pre and post Livaux consumption





Consumption significantly* increased (2-fold, 3.4% to 7%) the relative abundance of F. prau.

*P = 0.024, as determined by 16S rRNA gene sequencing, in functionally constipated participants



Consumption of kiwifruit capsules increases Faecalibacterium prausnitzii abundance in functionally constipated individuals in a double-blind, randomized, placebo-controlled trial.

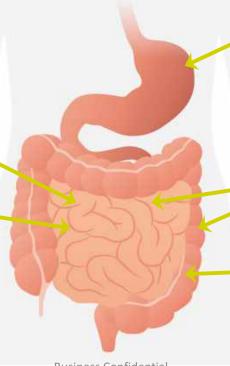
Blatchford, P., Stokolinski, H., Eady, S., Wallace, A., Butts, C., Gearry, R., Gibson, G., Ansell, J. (2017). Journal of Nutritional Science. DOI: 10.1017/jns.2017.52



Holistic Approach to Healthy Gut, & Healthy Immunity

- Gut transit time (PYY & PKC-α)
 - Improved digestion & nutrient absorption
- Inflammation (NO)
 - Improved intestinal premeability





- Protein digestion (actinidin)
 - Reduced bloating/discomfort
- Gastric emptying (GLP-1)
 - Improved digestion & nutrient absorption
- Mucus production (mucin 2)
- Enhanced gut protection
- Lubrication
- Faecal Bulking
 - Fibre swelling & water retention



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AIDP Range of Targeted Gut Health Ingredients











Material	Dose	Mechanism	Application	Clinical Studies	Cost/dose
Zespri® green kiwifruit powder	600 mg	Bowel regularity	Digestive Health	2 human 1 in silico	\$0.07
Zespri® gold kiwifruit powder	600 mg	Microbiome balance; Restoring F. prau	Digestive Health Immune Health Inflammation	2 human 1 in silico	\$0.07
XOS prebiotic	1 g	Metabolic reconditioning; Bifidogenic activity	Digestive Health Weight Management Blood Sugar/Lipids Metabolic Function	6+ human In-vivo In-vitro	\$0.03
GOS prebiotic	2 g	Microbiome fermentation; short chain FA production	Digestive Health Skin Health Beauty From Within Immune Health	2 human In vivo In vitro	\$0.03
Flavonoid-rich extract of G. glabra root	150 mg	Manage H. pylori; functional dyspepsia	Upper Digestive Tract Stomach Discomfort Dyspepsia	3 human	\$0.04