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Precision Prebiotics for Diverse Health Conditions

Dr. James DiNicolantonio
Director of Scientific Affairs

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The Importance of Microbiome Diversity

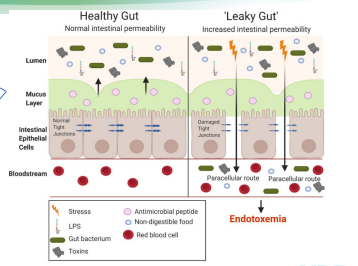
A Healthy Gut Environment

Diverse microbiome

Strong mucosal barrier + well-formed tight junctions within intestinal lining

Short chain fatty acid production

Protection from pathogens/LPS entering circulation
Reduced inflammation
Improved metabolic health
Weight management
Healthy immune function
Skin health
Cognition and mood support



Mohammad S, Thiemermann C. Role of Metabolic Endotoxemia in Systemic Inflammation and Potential Interventions. Front Immunol. 2021;11:594150. Published 2021 Jan 11. doi:10.3389/fimmu.2020.594150

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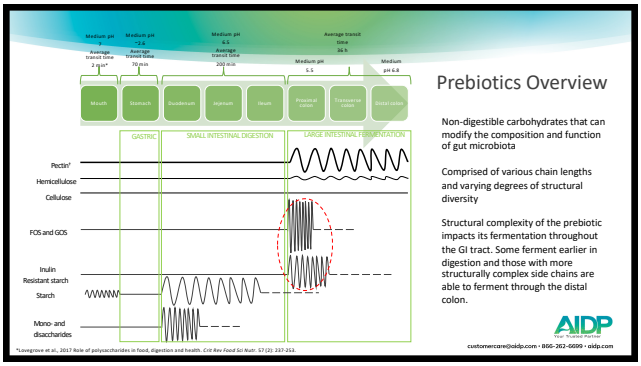

Prebiotics Overview

Non-digestible carbohydrates that can modify the composition and function of gut microbiota

Comprised of various chain lengths and varying degrees of structural diversity

Structural complexity of the prebiotic impacts its fermentation throughout the GI tract. Some ferment earlier in digestion and those with more structurally complex side chains are able to ferment through the distal colon.

*Lovegrove et al., 2017 Role of polysaccharides in food, digestion and health. *Crit Rev Food Sci Nutr.* 57 (2): 237-253.

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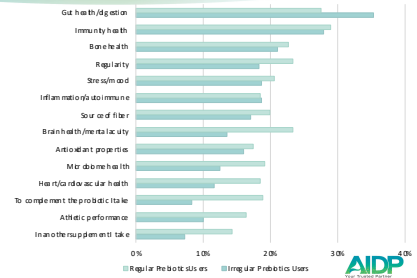
Why Consumers Take Prebiotics

INGREDIENT TRANSPARENCY CENTER

KEY ITC INSIGHTS:

- Regular prebiotics users choose these products for immunity and gut health, although are more spread out across all the choices
- Irregular users of prebiotics are using them largely for gut health
- Brain health has emerged as the third highest response for regular users, signaling awareness at least in general terms of the gut brain connection



ITC Insights: 2021 Consumer Supplement Survey

Note: Regular users indicated using supplement at least 4 times per week n=287. Irregular users n=461. Question: "Why are you taking a prebiotic supplement?"

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Precision Prebiotics

Alteration in gut composition, "selectivity" and host benefit are impacted by prebiotic structure.

Precision prebiotics have a higher specificity when feeding gut bacteria, leading to more selective alterations in the microbiome.

Key Advantages:

- ✓ Low dose
- ✓ Minimal side effects (bloating, discomfort)
- ✓ Selective growth of good bacteria
- ✓ Pleiotropic (anti-inflammatory) effects

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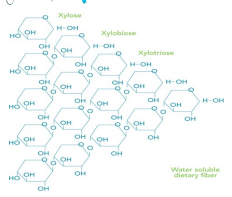
Low Dose XOS for Bifidogenic Reconditioning

PreticX Optimize Your Flora



- **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

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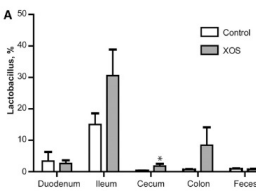
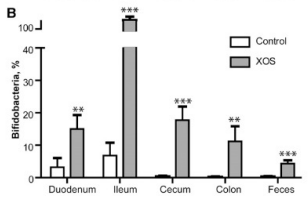
PreticX® selectively increases Bifidobacteria and Lactobacillus

Lactobacillus %



Bifidobacteria %



Dietary Xylooligosaccharide Downregulates IFN-gamma and the Low-Grade Inflammatory Cytokine IL-1B systemically in Mice. J of Nutrition. 2013

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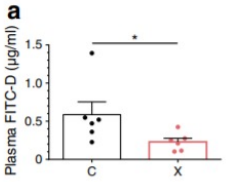
PreticX® Supports a Healthy Mucosal Barrier

Intake of XOS Improved Gut Barrier function



Spectrophotometric analysis of plasma FITC-dextran (FITCD) level 2 h post oral gavage at 7 weeks of age in (a) mice fed the control (C, n=6) or XOS (X, n=6) diet for their whole life

CF Hansen et al Diabetologia (2019) 62:1689–1700

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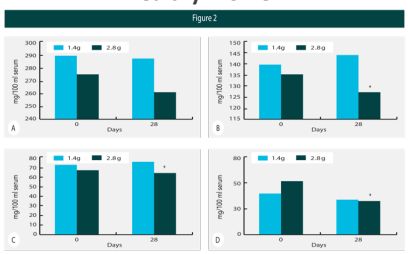
PreticX® Supplementation Improved Lipid Metabolism in Healthy Women



A: Total lipid, B: Cholesterol, C: Triglyceride, D; Glucose.
* p<0.05 day 28 versus day 0
Ha and Kim, *Korean J Nutr.* 2007; 40(2): 154 -161.

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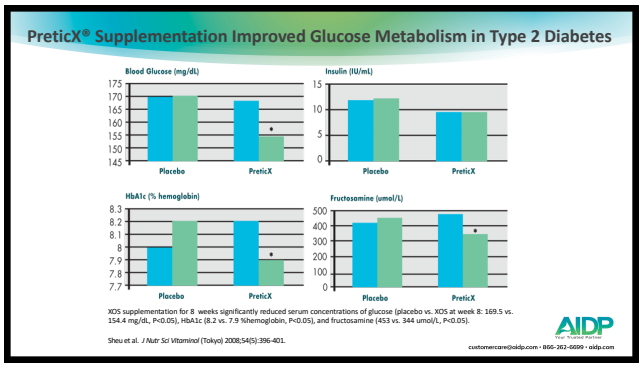
PreticX® Supplementation Improved Glucose Metabolism in Type 2 Diabetes
Blood Glucose (mg/dL)
175
170
165
160
155
150
145
Placebo
PreticX
Insulin (IU/mL)
15
10
5
0
Placebo
PreticX
HbA1c (% hemoglobin)
8.3
8.2
8.1
8
7.9
7.8
7.7
Placebo
PreticX
Fructosamine (umol/L)
500
400
300
200
100
0
Placebo
PreticX
XOS supplementation for 8 weeks significantly reduced serum concentrations of glucose (placebo vs. XOS at week 8: 169.5 vs. 154.4 mg/dL, P<0.05), HbA1c (8.2 vs. 7.9 %hemoglobin, P<0.05), and fructosamine (453 vs. 344 umol/L, P<0.05).
Sheu et al. J Nutr Sci Vitaminol (Tokyo) 2008;54(5):396-401.
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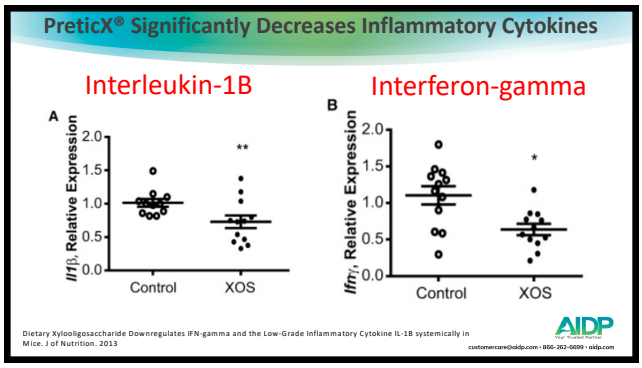
PreticX® Significantly Decreases Inflammatory Cytokines
Interleukin-1B
Interferon-gamma
A
Il1β, Relative Expression
2.0
1.5
1.0
0.5
0.0
**
Control
XOS
B
Ifnγ, Relative Expression
2.0
1.5
1.0
0.5
0.0
*
Control
XOS
Dietary Xylooligosaccharide Downregulates IFN-gamma and the Low-Grade Inflammatory Cytokine IL-1B systemically in Mice. J of Nutrition. 2013
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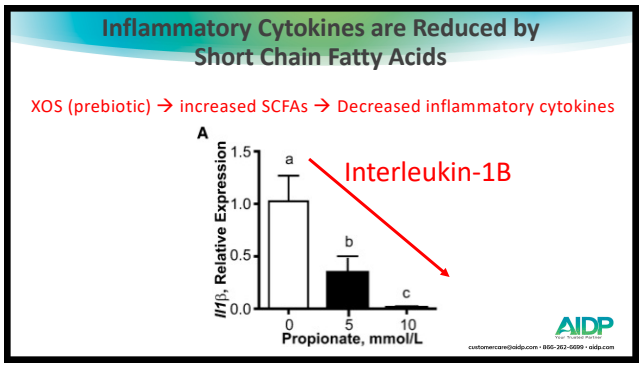
Inflammatory Cytokines are Reduced by Short Chain Fatty Acids
XOS (prebiotic) → increased SCFAs → Decreased inflammatory cytokines
A
Il1β, Relative Expression
1.5
1.0
0.5
0.0
a
b
c
Interleukin-1B
0
5
10
Propionate, mmol/L
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PreticX® Modulates Immune Markers

Xylo-oligosaccharides alone or in synbiotic combination with Bifidobacterium animalis subsp. lactis induce bifidogenesis and modulate markers of immune function in healthy adults: a double-blind, placebo-controlled, randomised, factorial cross-over study

Childs et al. British Journal of Nutrition (2014), 111, 1945–1956

Conclusion:

XOS supplementation significantly increased

- mean bowel movements
- bifidobacterial counts
- fasting plasma HDL concentrations.
- lower expression of the cell-surface markers CD16/56 on NKT cells
- lower IL-10 secretion
- increased participant-reported vitality and happiness.

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Gold Kiwifruit Powder with Specific *F. prau* Activity

- Derived from New Zealand **gold kiwifruit**
- Developed using proprietary, **pharmaceutical grade freeze-drying** method
- **Nutrient powerhouse:** rich in vitamin C, phenolic compounds and fiber
- **Prebiotic substrates** modulate the microbiome
- Kiwifruit dietary fiber mainly consists of **pectic polysaccharides** (pectin), hemicelluloses and cellulose.
- The most **fermentable** of these polysaccharides is pectin.
- Kiwifruit pectin is a prebiotic polysaccharide with a **complex and diverse structure.**
- Increases abundance of ***Faecalibacterium prausnitzii*** in the gut

Livaux
energise your gut

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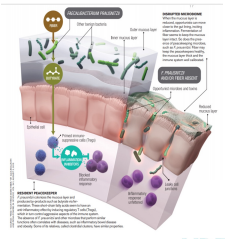
Faecalibacterium prausnitzii (F. prau)

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.



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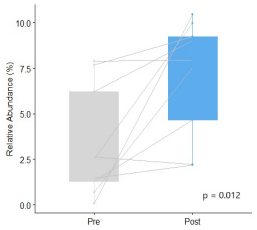
Livaux® Increases F. prau by More Than 100%

Relative Abundance of F. prau in Functionally Constipated Individuals (2.4 g Livaux/day for 4 weeks)



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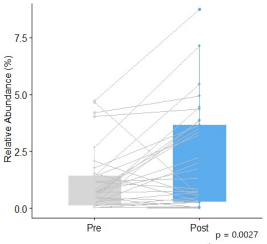
Livaux® Increases F. prau with Low Dose – Results of 2nd Clinical Trial

Relative Abundance of F. prau in Healthy Individuals (600 mg Livaux/day for 4 weeks)



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Gut Microbiota and Immunity – COVID-19 Study

Gut. 2021 Apr; 70(4): 698–706.
Published online 2021 Jan 11. doi: 10.1136/gutjnl-2020-323020
PMCID: PMC7804842
PMID: 33431578
Original research

Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19

Results

Gut microbiome composition was significantly altered in patients with COVID-19 compared with non-COVID-19 individuals irrespective of whether patients had received medication ($p<0.01$). Several gut commensals with known immunomodulatory potential such as *Faecalibacterium prausnitzii*, *Eubacterium rectale* and bifidobacteria were underrepresented in patients and remained low in samples collected up to 30 days after disease resolution. Moreover, this perturbed composition exhibited stratification with disease severity concordant with elevated concentrations of inflammatory cytokines and blood markers such as C reactive protein, lactate dehydrogenase, aspartate aminotransferase and gamma-glutamyl transferase.

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Study Significance and Future Implications

How might it impact on clinical practice in the foreseeable future?

- These findings suggest that depletion of immunomodulatory gut microorganisms contributes to severe COVID-19 disease.
- The dysbiotic gut microbiota that persists after disease resolution could be a factor in developing persistent symptoms and/or multisystem inflammation syndromes that occur in some patients after clearing the virus.
- Bolstering of beneficial gut species depleted in COVID-19 could serve as a novel avenue to mitigate severe disease, underscoring importance of managing patients' gut microbiota during and after COVID-19.

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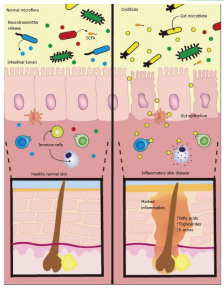
The Gut-Skin Connection



Imbalanced gut environment generates compounds and toxins that enter circulation and accumulate into the skin, causing:

- Inflammation
- Dryness
- Breakdown of collagen and elastin fibers
- Discoloration
- Appearance of fine lines and wrinkles

Vaughn AR, Notay M, Clark AK, Sivamani RK. Skin-gut axis: The relationship between intestinal bacteria and skin health. *World J Dermatol* 2017; 6(4): 52-58.

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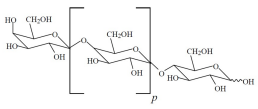
High-Purity GOS for Skin Health

Beauty OLIGO

is a unique, high purity, **LOW GLYCEMIC**, **GOS** proven to be effective in **SUPPORTING HEALTHY SKIN APPEARANCE**



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BeautyOLIGO® Skin Protective Effects in Animal Studies

IN VITRO AND ANIMAL STUDIES

INTERNATIONAL JOURNAL OF FOOD SCIENCES AND NUTRITION

Photoprotective effects of galacto-oligosaccharide and/or *Bifidobacterium longum* supplementation against skin damage induced by ultraviolet irradiation in hairless mice

Ki-Bae Hong[1], Mingeum Jeong[2], Ki Soo Han[2], Jae Hwan Kim[2], Yoahoon Park[1], and Hyung Joo Suh[1]

Control HC-GOS Bifdo HC-GOS+Bifdo

12 weeks

4 days irradiation

24 hour

Analysis

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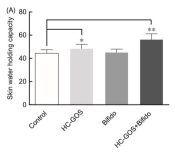
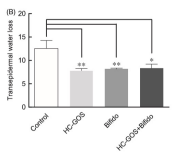
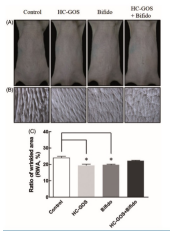
BeautyOLIGO® Skin Protective Effects in Animal Studies





Effect of GOS and/or Bifidobacterium on skin water-holding capacity (A) and transepidermal water loss (B) in UVB-irradiated hairless mice. Control: Saline; HC-GOS: GOS; Bifido: Bifidobacterium longum. Values mean±SE (n¼6), and compared to UV control at *p≤0.05 and **p≤0.01 using the Student's t-test.



Reduced wrinkle area in hairless mice after UV exposure with BeautyOLIGO® supplementation.

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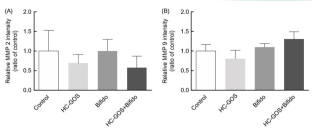
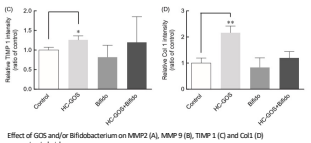
BeautyOLIGO® Mechanisms of Action





Effect of GOS and/or Bifidobacterium on MMP2 (A), MMP 9 (B), TIMP 1 (C) and Col1 (D) expression in hairless mouse.

Reduced Wrinkle Appearance

↑ Collagen Type 1/ TIMP 1

↓ MMP2/MMP9

Balanced Gut Environment

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BeautyOLIGO® Improves Skin Appearance

Dietary galactooligosaccharides improve skin health: a randomized double-blind clinical trial

Hong YH, Chang UJ, Kim YS, Jung EY, Suh HJ. *Asia Pac J Clin Nutr*. 2017;(26):4

- 84 healthy Korean volunteers
- 30–69 years of age
- fine wrinkles at the outer corner of the eyes
- 1.0 g of GOS or Placebo twice a day

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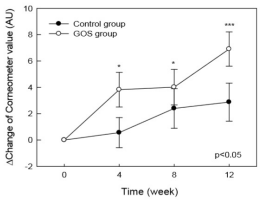
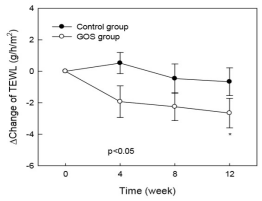
BeautyOLIGO® Improves Skin Hydration



Effects of galactooligosaccharides (GOS) on the Corneometer value in the healthy adults. The asterisks indicate significant differences (*p<0.05, ***p<0.001) between the baseline and the indicated week.



Effects of galactooligosaccharides (GOS) on transepidermal water loss (TEWL) in healthy adults. Asterisks indicate a significant difference (*p<0.05) between the baseline and the indicated week.

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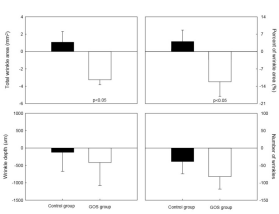
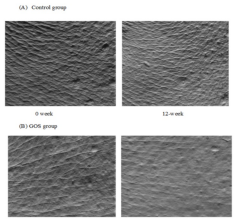
BeautyOLIGO® Reduces Appearance of Wrinkles



Effects of galactooligosaccharides (GOS) on wrinkle formation in healthy adults. The p values indicate a significant difference between changes in the two groups at each week by t test. All data were two-sided at the 5% significance level and are reported as mean±standard error of the mean.



Replica photography of crow's feet in healthy adults who received galactooligosaccharides (GOS) for 12 weeks.

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BeautyOLIGO® Supports Skin Tone - Hyperpigmentation

Inhibitory effect of galactooligosaccharide on skin pigmentation.
Prev. Nutr. Food Sci. 2019;24(3):321-326

In vitro study:
- effects of BeautyOLIGO on melanin accumulation in B16F10 cell model

Randomized, Double-Blind, Placebo Controlled Trial:
- N=79 (mean age 50-51 yrs)
- Placebo Group (n=39): 1 g dextrin 2x daily
- GOS Group (n=40): 1 g BeautyOLIGO 2x daily
- 12 weeks
- Changes in melanin index and erythema index

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BeautyOLIGO® Reduces Melanin and Erythema Index

Table 1. Changes in skin value indexes during 12 weeks of galactooligosaccharide (GOS) treatment

Variable	Group	Time (week)			
		Baseline	4	8	12
MI	Placebo (N=40)	160.08±4.28	159.53±4.05	154.72±3.92	155.65±4.13
	GOS (N=39)	161.84±5.57	158.42±4.48	145.85±4.94***††	145.55±5.03***††
EI	Placebo (N=40)	279.89±8.15	270.56±7.34	270.13±7.93	273.62±7.17
	GOS (N=39)	282.85±7.53	258.81±9.04***	253.57±9.30***†	253.85±8.11***†

Asterisk indicates a significant difference (***P<0.001) between baseline and change from baseline at each week, as calculated by a repeated measure ANOVA followed by Bonferroni-adjusted pairwise comparisons within groups. Significant differences were indicated by daggers (†P<0.05 and ††P<0.01 between changes in two groups at each week by t-test). Values are mean±SEM. MI, melanin index; EI, eythema index.

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