

Prebiotin Structure/Function Claim: Weight Management

Doc No.: VR003

Revision: 1

AUTHOR: Dr. Frank Jackson, MD

1. PURPOSE/SCOPE

The purpose of this document is to explain how Prebiotin plays a significant role in weight management and the clinical literature published in support of this structure/function claim.

This includes studies performed and an evaluation of the relevant scientific literature related to how prebiotin acts to help in weight management.

2. GENERAL DETAILS

2.1 Dietary Supplement Name

Proprietary Product Name:
Prebiotin

2.2 Manufacturer

Jackson GI Medical
1714 N. 2nd Street
Harrisburg, PA 17102
USA

2.3 Dietary Supplement Description

Oligofructose Enriched Inulin

3. BACKGROUND

Prebiotin, a Prebiotic Fiber Supplement offers a full-spectrum prebiotic (Oligofructose-Enriched-Inulin, or OEI). OEI is obtained by combining chicory long-chain inulin and oligofructose. Inulin and oligofructose belong to a class of carbohydrates known as fructans. Because of the beta-configuration of the anomeric C2 in their fructose monomers, inulin -type fructans resist hydrolysis by intestinal digestive enzymes, they classify as 'non-digestible' carbohydrates, and they are dietary fibers.

The main sources of inulin and oligofructose that are used in the food industry are chicory and Jerusalem artichoke. Inulin and oligofructose are considered as functional food ingredients since they affect the physiological and biochemical processes in rats and human beings, resulting in better health.

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Unlike ordinary prebiotics such as Inulin or FOS, OEI ensures that Prebiotin nourishes beneficial bacteria throughout the colon. OEI is also the most-researched prebiotic, used in many university and clinical studies.

A prebiotic has been defined as *'a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health.* Inulin and oligofructose are the best-studied prebiotics so far. They are selectively fermented by the microflora in the human colon leading to a bacterial composition that is dominated by bifidobacteria, a perceived health-promoting genus.

The National Cancer Institute defines OEI as:

A substance that is used to improve the health of the digestive system and bones and is being studied in the prevention of colon cancer. Oligofructose-enriched inulin is made by combining two substances that occur naturally in many plants, including chicory root, wheat, bananas, onion, and garlic. Oligofructose-enriched inulin helps healthy bacteria grow in the intestines and helps the body absorb calcium and magnesium. OEI is also called Raftilose Synergy.

Source: (<http://www.cancer.gov/dictionary>)

OEI or oligofructose supplementation has a potential benefit in promoting weight management as evident in the way it positively affects the beneficial bacteria in the colon. A bad bacterial makeup in the colon has the potential to hinder weight management.

4. PUBLISHED LITERATURE

4.1 Literature Search

A literature search was conducted using PubMed and Medline to identify articles that contained studies on prebiotin (oligofructose enriched inulin) related to the weight management, obesity and metabolic disorders. Additionally, the microbiome was searched as this is referred to as the huge bacterial complex that resides within the colon and how important this incredibly complex mix of bacteria is important in the fight against obesity.

The following articles support the function claim that a healthy microbiota provided by prebiotics in the diet supports weight management. The articles and/or studies listed in Table 1 are summarized individually.

Table 1 Clinical Literature

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	Author	Source/Published	Title of Publication	Year of Publication
1	Ley RE, Bäckhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JL.	Proc Natl Acad Sci U S A. 2005 Aug 2;102(31):11070-5.	Obesity alters gut microbial ecology.	2005
2	Chen J, He X, Huang J.	Journal of Food Science 2014 Apr;79(4):R442-51. doi: 10.1111/1750-3841.12397.	Diet effects in gut microbiome and obesity.	2014
3	Luoto R ¹ , Collado MC, Salminen S, Isolauri E.	Ann Nutr Metab. 2013;63 Suppl 2:17-26. doi: 10.1159/000354896.	Reshaping the gut microbiota at an early age: functional impact on obesity risk?	2013
4	Parekh PJ, Arusi E, Vinik AI, Johnson DA	Front Endocrinol (Lausanne). 2014 Apr 7;5:47. eCollection 2014.	The Role and Influence of Gut Microbiota in Pathogenesis and Management of Obesity and Metabolic Syndrome.	2014
5	Roberfroid M ¹ , Gibson GR, Hoyles L, McCartney AL, Rastall R, Rowland I, Wolvers D, Watzl B, Szajewska H, Stahl B, Guarner F, Respondek F, Whelan K, Coxam V, Davicco MJ, Léotoing L, Wittrant Y, Delzenne NM, Cani PD, Neyrinck AM, Meheust A.	British Journal of Nutrition 2010 Aug;104 Suppl 2:S1-63. doi: 10.1017/S0007114510003363.	Prebiotic effects: metabolic and health benefits.	2010
6	Caricilli AM, Saad MJ.	Curr Opin Clin Nutr Metab Care. 2014 Jul;17(4):312-318.	Gut microbiota composition and its effects on obesity and insulin resistance.	2014
	Xiao S, Fei N, Pang X, Shen J, Wang L, Zhang B, Zhang M, Zhang X, Zhang C, Li M, Sun L,	FEMS Microbiol Ecol. 2014 Feb;87(2):357-67. doi: 10.1111/1574-6941.12228.	A gut microbiota-targeted dietary intervention for amelioration of chronic	2014

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	Author	Source/Published	Title of Publication	Year of Publication
	Xue Z, Wang J, Feng J, Yan F, Zhao N, Liu J, Long W, Zhao L.		inflammation underlying metabolic syndrome.	

Article #1

Obesity alters gut microbial ecology.

Ley RE, Bäckhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JI.

Author information

Center for Genomes Sciences, Washington University School of Medicine, St. Louis, MO 63108, USA.

ABSTRACT

We have analyzed 5,088 bacterial 16S rRNA gene sequences from the distal intestinal (cecal) microbiota of genetically obese ob/ob mice, lean ob/+ and wild-type siblings, and their ob/+ mothers, all fed the same polysaccharide-rich diet. Although the majority of mouse gut species are unique, the mouse and human microbiota(s) are similar at the division (superkingdom) level, with Firmicutes and Bacteroidetes dominating. Microbial-community composition is inherited from mothers. However, compared with lean mice and regardless of kinship, ob/ob animals have a 50% reduction in the abundance of Bacteroidetes and a proportional increase in Firmicutes. These changes, which are division-wide, indicate that, in this model, obesity affects the diversity of the gut microbiota and suggest that intentional manipulation of community structure may be useful for regulating energy balance in obese individuals. The sequences reported in this paper have been deposited in the GenBank database [accession nos. DQ 014552--DQ 015671 (mothers) and AY 989911--AY 993908 (offspring)].

<http://www.ncbi.nlm.nih.gov/pubmed/16033867>

Article #2

Diet effects in gut microbiome and obesity.

Chen J, He X, Huang J.

Author information

School of Chemical Engineering & Technology, Tianjin Univ, Tianjin, 300072, China.

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ABSTRACT

The 100 trillion microbes in human gut coevolve with the host and exert significant influences on human health. The gut microbial composition presents dynamic changes correlated with various factors including host genotypes, age, and external environment. Effective manipulation of the gut microbiota through diets (both long-term and short-term diet patterns), probiotics and/or prebiotics, and antibiotics has been proved being potential to prevent from metabolic disorders such as obesity in many studies. The dietary regulation exerts influences on microbial metabolism and host immune functions through several pathways, of which may include selectively bacterial fermentation of nutrients, lower intestinal barrier function, overexpression of genes associated with disorders, and disruptions to both innate and adaptive immunity. Discoveries in the interrelationship between diet, intestinal microbiome, and body immune system provide us novel perceptions to the specific action mechanisms and will promote the development of therapeutic approaches for obesity.

<http://www.ncbi.nlm.nih.gov/pubmed/24621052>

Article #3

Reshaping the gut microbiota at an early age: functional impact on obesity risk?

Luoto R, Collado MC, Salminen S, Isolauri E.

Author information

Department of Pediatrics and Adolescent Medicine, Turku University Hospital, Turku, Finland.

ABSTRACT

Overweight and obesity can currently be considered a major threat to human health and well-being. Recent scientific advances point to an aberrant compositional development of the gut microbiota and low-grade inflammation as contributing factors, in conjunction with excessive energy intake. A high-fat/energy diet alters the gut microbiota composition, which reciprocally engenders excessive energy harvesting and storage. Further, microbial imbalance increases gut permeability, leading to metabolic endotoxemia, inflammation and insulin resistance. Local intestinal immunologic homeostasis is achieved by tolerogenic immune responses to microbial antigens. In the context of amelioration of insulin sensitivity and decreased adiposity, the potential of gut microbiota modulation with specific probiotics and prebiotics lies in the normalization of aberrant microbiota, improved gut barrier function and creation of an anti-inflammatory milieu. This would suggest a role for probiotic/prebiotic interventions in the search for preventive and therapeutic applications in weight management.

<http://www.ncbi.nlm.nih.gov/pubmed/24217033>

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Article #4

The Role and Influence of Gut Microbiota in Pathogenesis and Management of Obesity and Metabolic Syndrome.

Parekh PJ, Arusi E, Vinik AI, Johnson DA

Author information

- Department of Internal Medicine, Eastern Virginia Medical School , Norfolk, VA , USA.
- Endocrinology Division, Department of Internal Medicine, Eastern Virginia Medical School , Norfolk, VA , USA.
- Gastroenterology Division, Department of Internal Medicine, Eastern Virginia Medical School , Norfolk, VA , USA.

ABSTRACT

The obesity epidemic has drastically impacted the state of health care in the United States. Aside from poor diet hygiene and genetics, there are many other factors thought to play a role in the emergence of obesity and the metabolic syndrome. There has been a paradigm shift toward further investigating the gut microbiota and its implications in the pathogenesis of a variety of disease states, including inflammatory bowel disease, *Clostridium difficile*, and most recently obesity and the metabolic syndrome. This article is intended to evaluate the role of gut microbiota in the pathogenesis of obesity and metabolic syndrome and its influence in future management.

<http://www.ncbi.nlm.nih.gov/pubmed/24778627>

Article #5

Prebiotic effects: metabolic and health benefits.

Roberfroid M¹, Gibson GR, Hoyles L, McCartney AL, Rastall R, Rowland I, Wolvers D, Watzl B, Szajewska H, Stahl B, Guarner F, Respondek F, Whelan K, Coxam V, Davicco MJ, Léotoing L, Wittrant Y, Delzenne NM, Cani PD, Neyrinck AM, Meheust A.

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ABSTRACT

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The different compartments of the gastrointestinal tract are inhabited by populations of micro-organisms. By far the most important predominant populations are in the colon where a true symbiosis with the host exists that is a key for well-being and health. For such a microbiota, 'normobiosis' characterises a composition of the gut 'ecosystem' in which micro-organisms with potential health benefits predominate in number over potentially harmful ones, in contrast to 'dysbiosis', in which one or a few potentially harmful micro-organisms are dominant, thus creating a disease-prone situation. The present document has been written by a group of both academic and industry experts (in the ILSI Europe Prebiotic Expert Group and Prebiotic Task Force, respectively). It does not aim to propose a new definition of a prebiotic nor to identify which food products are classified as prebiotic but rather to validate and expand the original idea of the prebiotic concept (that can be translated in 'prebiotic effects'), defined as: 'The selective stimulation of growth and/or activity(ies) of one or a limited number of microbial genus(era)/species in the gut microbiota that confer(s) health benefits to the host.' Thanks to the methodological and fundamental research of microbiologists, immense progress has very recently been made in our understanding of the gut microbiota. A large number of human intervention studies have been performed that have demonstrated that dietary consumption of certain food products can result in statistically significant changes in the composition of the gut microbiota in line with the prebiotic concept. Thus the prebiotic effect is now a well-established scientific fact. The more data are accumulating, the more it will be recognised that such changes in the microbiota's composition, especially increase in bifidobacteria, can be regarded as a marker of intestinal health. The review is divided in chapters that cover the major areas of nutrition research where a prebiotic effect has tentatively been investigated for potential health benefits. The prebiotic effect has been shown to associate with modulation of biomarkers and activity(ies) of the immune system. Confirming the studies in adults, it has been demonstrated that, in infant nutrition, the prebiotic effect includes a significant change of gut microbiota composition, especially an increase of faecal concentrations of bifidobacteria. This concomitantly improves stool quality (pH, SCFA, frequency and consistency), reduces the risk of gastroenteritis and infections, improves general well-being and reduces the incidence of allergic symptoms such as atopic eczema. Changes in the gut microbiota composition are classically considered as one of the many factors involved in the pathogenesis of either inflammatory bowel disease or irritable bowel syndrome. The use of particular food products with a prebiotic effect has thus been tested in clinical trials with the objective to improve the clinical activity and well-being of patients with such disorders. Promising beneficial effects have been demonstrated in some preliminary studies, including changes in gut microbiota composition (especially increase in bifidobacteria concentration). Often associated with toxic load and/or miscellaneous risk factors, colon cancer is another pathology for which a possible role of gut microbiota composition has been hypothesised. Numerous experimental studies have reported reduction in incidence of tumours and cancers after feeding specific food products with a prebiotic effect. Some of these studies (including one human trial) have also reported that, in such conditions, gut microbiota composition was modified (especially due to increased concentration of bifidobacteria). Dietary intake of particular food products with a prebiotic effect has been shown, especially in adolescents, but also tentatively in postmenopausal women, to increase Ca absorption as well as bone Ca accretion and bone mineral density. Recent data, both from experimental models and from human studies, support the beneficial effects of particular food products with prebiotic properties on energy homeostasis, satiety regulation and body weight gain. Together, with data in obese animals and patients, these studies support the hypothesis that gut

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microbiota composition (especially the number of bifidobacteria) may contribute to modulate metabolic processes associated with syndrome X, especially obesity and diabetes type 2. It is plausible, even though not exclusive, that these effects are linked to the microbiota-induced changes and it is feasible to conclude that their mechanisms fit into the prebiotic effect. However, the role of such changes in these health benefits remains to be definitively proven. As a result of the research activity that followed the publication of the prebiotic concept 15 years ago, it has become clear that products that cause a selective modification in the gut microbiota's composition and/or activity(ies) and thus strengthens normobiosis could either induce beneficial physiological effects in the colon and also in extra-intestinal compartments or contribute towards reducing the risk of dysbiosis and associated intestinal and systemic pathologies.

<http://www.ncbi.nlm.nih.gov/pubmed/20920376>

Article #6

Gut microbiota composition and its effects on obesity and insulin resistance.

Caricilli AM, Saad MJ.

Author information

Department of Internal Medicine, State University of Campinas, Campinas, Sau Paulo, Brazil.

ABSTRACT

PURPOSE OF REVIEW:

Rising evidence suggest that variation in the gut microbiome at gene and species levels defines subsets of individuals who have increased risk of obesity-related metabolic disorders, including insulin resistance and type 2 diabetes, which is influenced by diet and genetic profile of the host. Our goal in this review is gathering the newest findings concerning gut microbiota composition and effects on host's metabolism.

RECENT FINDINGS:

Dietary changes have been shown as the most prominent shaper of gut microbiota composition, reflecting major phenotypes, which can also be transmitted to other individuals, in spite of genetic variances. Gut microbiota composition has also been presented as diversity, which may have important implications in metabolite production and consequent interference with inflammatory activation, insulin resistance, and obesity.

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SUMMARY:

Specific approaches made it possible to comprehend some of the interactions between certain bacterial strains and their host, and how their metabolites may interfere with host's cell signaling, changing its metabolic profile. Herein, we discuss some of the mechanisms by which alterations in the gut microbiota composition may contribute to the pathophysiology of obesity and its related co-morbidities.

<http://www.ncbi.nlm.nih.gov/pubmed/24848531>

Article #7

A gut microbiota-targeted dietary intervention for amelioration of chronic inflammation underlying metabolic syndrome.

Xiao S, Fei N, Pang X, Shen J, Wang L, Zhang B, Zhang M, Zhang X, Zhang C, Li M, Sun L, Xue Z, Wang J, Feng J, Yan F, Zhao N, Liu J, Long W, Zhao L.

Author information

State Key Laboratory of Microbial Metabolism, School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai, China.

ABSTRACT

Chronic inflammation induced by endotoxin from a dysbiotic gut microbiota contributes to the development of obesity-related metabolic disorders. Modification of gut microbiota by a diet to balance its composition becomes a promising strategy to help manage obesity. A dietary scheme based on whole grains, traditional Chinese medicinal foods, and prebiotics (WTP diet) was designed to meet human nutritional needs as well as balance the gut microbiota. Ninety-three of 123 central obese volunteers (BMI ≥ 28 kg m⁻²) completed a self-controlled clinical trial consisting of 9-week intervention on WTP diet followed by a 14-week maintenance period. The average weight loss reached 5.79 ± 4.64 kg ($6.62 \pm 4.94\%$), in addition to improvement in insulin sensitivity, lipid profiles, and blood pressure. Pyrosequencing of fecal samples showed that phylotypes related to endotoxin-producing opportunistic pathogens of Enterobacteriaceae and Desulfovibrionaceae were reduced significantly, while those related to gut barrier-protecting bacteria of Bifidobacteriaceae increased. Gut permeability, measured as lactulose/mannitol ratio, was decreased compared with the baseline. Plasma endotoxin load as lipopolysaccharide-binding protein was also significantly reduced, with concomitant decrease in tumor necrosis factor- α , interleukin-6, and an increase in adiponectin. These results suggest that modulation of the gut microbiota via dietary intervention may enhance the intestinal barrier integrity, reduce circulating antigen load, and ultimately ameliorate the inflammation and metabolic phenotypes.

<http://www.ncbi.nlm.nih.gov/pubmed/24117923>

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5. DATA SUMMARY – CLINICAL LITERATURE

Based on the clinical literature and research presented, prebiotin, oligofructose-enriched inulin has been shown to have a role in weight management through nourishing beneficial bacteria throughout the colon. Based on studies and literature, prebiotic properties have been shown to have an effect on energy homaeostasis, satiety regulation and body weight gain.

6. ATTACHMENTS

6.1 Clinical Literature referenced is maintained in the Structure/Function Technical File for Weight Management.

APPROVALS:

CEO: _____ Date _____

COO: _____ Date _____

QUALITY/REGULATORY: _____ Date _____