nexira
Innovation Inspired by Nature

Fibregum™, a healthy, natural and gentle fiber with comfortable digestibility

Digestive tract and well-being

A healthy digestive tract is characterized by the ability to process nutrients through the digestive tract in an efficient manner, in order to correctly nourish the entire organism.
People who suffer from an unhealthy digestive tract experience uncomfortable conditions including heart burn, gas, constipation, diarrhea, nausea, abdominal pain and flatulence.
Digestive discomfort can be highly debilitating with a strong impact on overall well-being and quality of life.

Health benefits of a diet rich in fiber

The advantage of a diet rich in fiber is not only related to the digestive process but also to an increase of bulk, softened stool and a shorter time through the intestinal tract. Fibers are considered to increase stool production, to prevent constipation, and may have some prevention effects on colorectal cancer. They also increase satiety sensation which reduces calorie intake; consequently, they may have some benefits for weight management.
Moreover, soluble dietary fibers could enable additional positive health activities including colic fermentation stimulation, reduction of cholesterolemia and a reduction of post-pandrial glycemia and / or insulin.

Dietary fiber, a wide range of components, soluble and insoluble fibers

According to the American Food and Nutrition Board, functional fibers are isolated glycosides, that are nondigestible and promote physiological benefits in humans. Dietary fibers could also be defined as plant and animal derived components that are able to resist to the enzymatic degradation in the digestive tract of humans.

Fibers are divided in two groups:
- Soluble fibers that are able to dissolve in water
- Insoluble fibers that are not able to dissolve in water but can absorb it.

Energy, caloric value

Fibers provide less energy than sugars or starches because they are not fully absorbed by the human body. Insoluble fibers are not transformed during digestion, so they are not absorbed and provide no energy. Soluble fibers, are fermented or partially fermented by the gut flora thus contributing to some increased energy.

Prebiotic effect

Prebiotics are defined as non-digestible food compounds that are selectively fermented, and which confer benefits by inducing specific changes, both in the composition and/or in the activity of the gastrointestinal microbiota[1]. Lactobacilli and bifidobacteria are considered indicators of prebiotic stimulation with Bifidobacteria being

the most significant organisms for gut health[II]. As an example, the fermentation of acacia gum in the large bowel stimulates the growth of these bacteria. Soluble fiber could stimulate colic fermentation and thus Short Chain Fatty Acids (SCFAs) production such as propionate and butyrate. SCFAs are the main products of the colonic bacterial fermentation of dietary fiber and the main organic anions in the colon. They may have many benefits on the digestive tract[III].

Prebiotic effects in the gut can be evaluated by assessing the increased or decreased production of health related bacterial metabolites, growth of health promoting bacteria and a decrease in intestinal pathogens[IV].

Side effects

The American Diabetes Association and WHO agree that dietary fiber intake should be near 25-30 g/day for a healthy life style. A study showed that mean daily dietary fiber intake for 2007-2008 was 15.9 g/day[V].

But consuming dietary fiber may have potential digestive side effects. This is often the case for some fibers as a result of their fermentation mechanism. Fiber fermentation produces gas, and some fibers are rapidly fermented and are associated with a "high" gas production[VI]. In that case, they may induce undesirable manifestations including bloating, abdominal cramps, flatulence and diarrhea. However, one of the main concerns of nutritionists and healthy food producers is to provide high fiber diet and meals that could provide a sufficient dose of fiber without side effects. Thus, the goal is to reach improved digestive tolerance offering products with no adverse events that could limit their consumption.

Consumers have a more curative than preventive attitude regarding their digestive health. Half of the people are interested in preventive measures and six out of ten people are interested in drinks and snacks for a better digestive health (Mintel). Many diseases are related to gastrointestinal health notably obesity. More than a third of U.S. adults (34.9%) are obese and the estimated annual medical cost was $ 147 billion in 2008 [3]:

Obesity itself can lead to other diseases such as cardiovascular disease, certain types of cancer and type 2 diabetes [3]:

- As an example, colorectal cancer is the second leading cause of cancer death in the United States and the third most common cancer in men and women. [3]
- Other diseases or syndromes are also largely related to gastrointestinal diseases. Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder with prevalence rates in the world ranging from 9-23%. Most people with IBS have mild symptoms that do not allow them to immediately recognize that they are suffering from IBS. However, the number of annual physician visits for IBS reasons varies from 2.4 to 3.5 million and IBS is the most commonly diagnosed disorder by gastroenterologists.[4]
- Other serious diseases such as Crohn's disease, ulcerative colitis and inflammatory bowel disease (IBD) are also listed. IBD includes chronic or recurring immune response and inflammation of the gastrointestinal tract. 1.4 million US people suffer from diseases like IBD. [3]

Some non-transmissible diseases are related to the consumption of diets poor in fiber.

Figure 1: Incidence of some epidemiologic diseases

	Number of cases (million)	Year of assessment	Sources
Colorectal cancer	1.24	2008	Cancer search UK[5]
Diabetes	347.00		World Health Organization[6]
Obesity	500.00	2008	World Health Organization[7]
Cardiovascular diseases	17.30	2008	World Health Organization[8]

3. Centers for Disease Control and Prevention
4. International Foundation for Functional Gastrointestinal Disorders
5. www.cancerresearchuk.org/cancer-info/cancerstats/world/colorectal-cancer-world/, consulted on 14/01/08
6. www.who.int/mediacentre/factsheets/fs312/en/, consulted on 14/01/08
7. www.who.int/mediacentre/factsheets/fs311/en/, consulted on 14/01/08
8. www.who.int/mediacentre/factsheets/fs317/en/, consulted on 14/01/08

Fibregum™

Fibregum™ is an all natural, GMO-free source of soluble dietary fiber, obtained from carefully selected acacia gum sap exuded from the stems and branches of acacia trees.

Fibregum™ offers a guaranteed minimum of 90% soluble fiber on a dry weight basis, using the traditional testing method AOAC 985.29. It is a non-digestible, high molecular weight polysaccharide.

It is composed of a proteinaceous core and associated polysaccharidic fractions. It is made up of neutral sugars and uronic acids (95 % of the dry matter), protein (1% to 2% (depending on the species), polyphenols (catechins, epicathechins, etc.), and minerals (magnesium, potassium, calcium, sodium). It has a very complex structure with an average molecular weight varying from 300 to 800 kDa.

Demonstration of the comfortable digestibility of Fibregum™

Many studies have demonstrated Fibregum™ benefits on the digestive tract.

Study 1: Fibregum™ intestinal tolerance

In 2003 Cherbut et al[VII] carried out an experiment to determine Fibregum™ intestinal tolerance in comparison with sucrose (neutral reference) and short-chain fructo-oligosaccharide (FOS), a well-known prebiotic fiber.

This study reported that Fibregum™ did not induce adverse gastrointestinal effects even when consumed at high doses, and demonstrates that it is a bifidogenic factor.

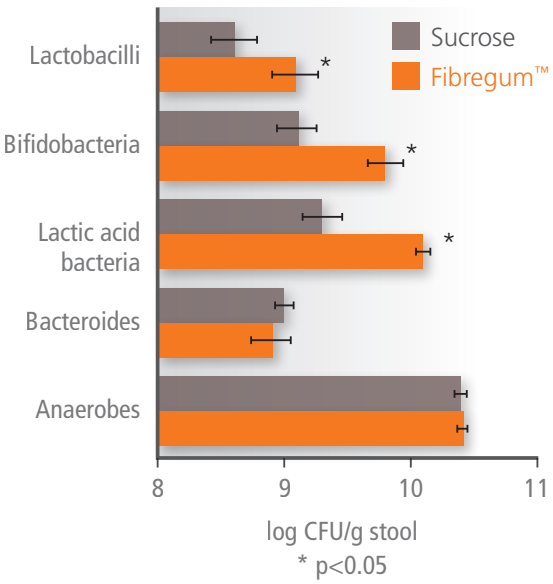
The study also showed a high digestive tolerance of Fibregum™. Flatulence, bloating and borborygmi occurred at lower doses with FOS than with Fibregum™. The main complaint related to FOS was excessive flatulence: daily doses below 20 g/day resulted in only minor complaints while doses of 50 g/day resulted in abdominal cramps and diarrhea.

In this first study, Fibregum™ did not induce flatulence below the dose of 30 g/day and daily doses higher than 50 g/day did not provoke any abdominal cramps or diarrhea. Related digestive symptoms mean occurrence and 50% effective dose (ED50) are summarized in *figure 2: "Mean occurrence and 50% effective dose (ED50)"*. The study also demonstrated that Fibregum™ stimulates the growth of lactic acid bacteria as shown in *figure 3: "Increase of LAB with Fibregum™ (10 g/d) compared to control (10 g/d)"*.

Figure 2: Mean occurrence and 50% effective dose (ED50)

Symptom	Occurrence dose (g/day)		ED50 (g/day)	
	AG	FOS	AG	FOS
Flatus	53.5±2.5	26.5±2.1	46	17.5
Bloating	67±2.1	50±3.1	65.7	41.7
Borborygmi	70.5±2.2	51.5±3.3	60.7	60
Cramps	71±1.9	67.8±2.1	55	57.5

Figure 3: Clinical study on healthy volunteers. Increase of LAB with Fibregum™ (10 g/d) compared to control (10 g/d)



Study 2: Fibregum™ decreases FOS side effects

In 2008 Goetze et al[VIII] conducted an experiment to assess how partial replacement of FOS by Fibregum™ may attenuate side effects. They compared the side effects of FOS versus a blend of 50% FOS and 50% Fibregum™. The study showed that FOS generates more abdominal side effects than Fibregum™. Both products, FOS and blend, significantly increased the scores for bloating and gas production. Borborygmi were also significantly increased under FOS consumption. Moreover, there was a tendency for increased scores for belching and 'general' impairment under FOS only. Blend did show a slightly lower side-effect profile in comparison with FOS which supports the difference in the comfort's digestion of FOS compared to Fibregum™ and that the addition of Fibregum™ to FOS could minimize FOS side effects.

Fibregum™ present a negligible glycaemic index because it is not digested in the small intestine. The caloric value varies between 1 and 2 kcal/g depending on the country.

Study 3: Progressive fermentation of Fibregum™

To further understand the intestinal tolerance of Fibregum™, Nexira conducted an in vitro experiment whose results were published in 2013[IX].

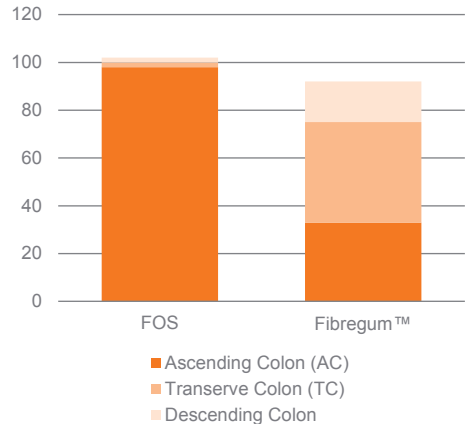
The Simulator of the Human Intestinal Microbial Ecosystem (SHIME®) was used in order to compare the Fibregum™ and the FOS digestion. This device mimics the human gastrointestinal digestive tract*.

The study showed that FOS boosted the fermentation in the ascending colon while Fibregum™ was more gradually fermented in the distal colon.

This data was confirmed by the results of the Size Exclusion Chromatography (SEC) analysis as shown on *figure 4: "Comparative fermentation in AT, TC and DC for FOS vs Fibregum™"*. Data are presented per week in the ascending colon (AC), transversal colon (TC) and distal colon (DC). FOS was quickly fermented in the simulated ascending colon compartment, while part of Fibregum™ is not metabolized in the upper digestive tract and is not hydrolyzed in the small intestine, due to a lack of proper depolymerizing enzymes such as galactanases or arabinases. It is only fermented by lactic bacteria in the large bowel. The study showed that Fibregum™ was fermented in the transverse colon and a residual part was still available for fermentation in the distal colon. It was possible to observe an adaptation of the metabolism of bacteria that increased their capability in fermenting Fibregum™ during the 3 weeks of treatment. In fact, the residual amount of the product available after fermentation constantly decreased during the 3 weeks of treatment, comparing a given colon compartment with the respective one 2 weeks earlier.

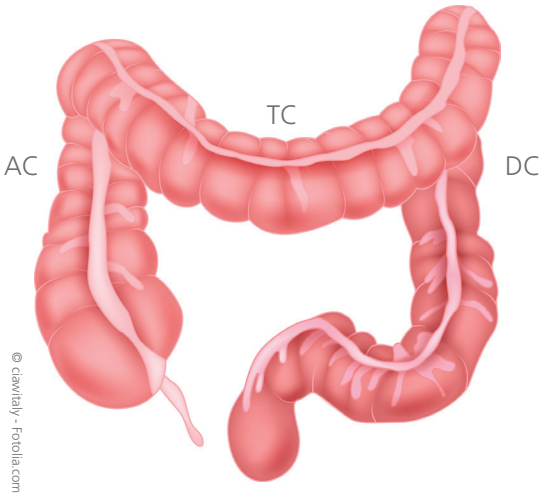
**This device is a continuous model that allows the in-depth study of the biological activity of selected molecules in the gut, under representative environmental conditions and under long-term repeated administration conditions. This technology platform allows validation of functional properties of food products in the human gastrointestinal tract, performing mechanistic studies in areas of the gut that are not easily accessible in in-vivo trials therefore providing useful complementary.*

Figure 4: Comparative fermentation in AT, TC and DC for FOS vs Fibregum™



Quantity of carbohydrate digested in regard to the three parts of the colon. % refers to the initial amount that was dosed in the SHIME device.

Figure 5: Colon illustration



A short-term measurement (up to 48 h) of gas production confirmed the fast fermentation of FOS as compared with Fibregum™.

SEC analysis also showed that the efficiency of Fibregum™ usage by bacteria increased during the 3 weeks of treatment, an adaptation property in compliance with what Angelakis and colleagues (2012)[X] describe in their review about high or low-fiber diets.

Conclusion

This technical paper showed the excellent tolerance of Fibregum™.

This tolerance is most notably due to the slow fermentation of Fibregum™ by the gut microflora. This gradual fermentation and high tolerability makes Fibregum™ a very potent tool to increase fiber diet content, even for people with high digestive discomfort such as IBS or fructose malabsorption[XI].

Thanks to all its properties, Fibregum™ may improve intestinal well-being, health, and may be a potential nutrient to regulate gut microbiota homeostatis.

I Roberfroid, M. (2007) Prebiotics ; the concept revisited. J Nutr 137: 830S-837S

II Gibson GR & Roberfroids MB (1995) Dietary modulation of the human colonic microbiota : introducing the concept of prebiotics. J Nutr 125, 1401-1412.

III Aube A-C, Cherbut C, Galmiche J-P (1995) Acides gras à chaîne courte : rôle en pathogénie intestinale et potentiel thérapeutique en gastroentérologie. Hépato-Gastro. Volume 2, Numéro 5, 447-55, Septembre - Octobre 1995, Bases fondamentales… en physiologie.

IV EFSA Gut Guidance http://www.efsa.europea.eu/en/supporting/pub/136e.htm

V J Acad Nutr Diet. 2012 May;112(5):642-8. doi: 10.1016/j.jand.2012.01.019. Epub 2012 Apr 25. Trends in dietary fiber intake in the United States, 1999-2008. King DE1, Mainous AG 3rd, Lambourne CA

VI Grimble, G. (1989) Fiber, fermentation, flora, and flatus. Gut 30, 6-13.

VII Cherbut C, Michel C, Raison V, Kravtchenko T & Severine M (2003) Accacia gum is a bifidogenic dietary fiber with high digestive tolerance in healthy humans. Microbial Ecol Health Dis 15, 43–50.

VIII Goetze O, Fruehauf H, Pohl D, Giarre M, Rochat F, Ornstein K, Menne D, Fried M and Thumshirn M (2008) Effect of a prebiotic mixture on intestinal comfort and general wellbeing in health. Br J Nutr 100, 1077-1085.

IX Terpend K, Possemiers S, Daguet D and Marzorati M (2013) Arabinogalactan and fructo-oligosaccharides have a different fermentation profile in the Simulator of the Human Intestinal Microbial Ecosystem (SHIME®). Environ Microbiol Rep Aug;5(4):595-603.

X Angelakis, E., Armougom, F., Million, M., and Raoult, D. (2012) The relationship between gut microbiota and weight gain in humans. Future Microbiol 7: 91–109.

XI www.foodintol.com/fructose-intolerance/fructose-malabsorption, consulted on 14/01/30