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Easy-to-Digest inavea™ PURE ACACIA and BAOBAB + ACACIA: Organic, All-Natural Prebiotics For Gut Health

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Introduction

Today's consumers are more attentive to their diet and its effects on their overall health and well-being. According to FMCG Guru, 68% of consumers recognize the link between good digestive health and good overall health. The digestive health category is on the rise: In 2019, it was +6% in France, and +8% in the USA. Consumers worldwide are increasingly seeking natural products, with a shorter and cleaner ingredient list [no synthetics, no additives, GMO-free]. As they adapt a healthier diet, they reach for organically-produced foods that are free from certain components, including things such as sugar, hydrogenated fat, salt, gluten, and lactose. From another crucial perspective, they wish to consume foods that contain ingredients such as prebiotics, including natural fibers that can be beneficial to their gut health. **inavea™ PURE ACACIA and inavea™ BAOBAB + ACACIA** are organic formulations that provide a synergistic, prebiotic effect on digestive health.

Every day, 70 million people are subject to digestive discomfort.[1] Irritable bowel syndrome [IBS] is the most highly diagnosed functional gastrointestinal disorder, affecting between 10% to 15% of the population worldwide. In the Digestive Health category, the demand for efficacious prebiotic ingredients is quickly rising, due to a diversity of market drivers. Consumers are aware of the multiple health benefits of a well-balanced microbiota, and digestive health is often associated with immunity because of its link with the gut barrier; consuming prebiotics can be considered a means of prevention.

A 2019 consumer study demonstrated that Prebiotics are generally associated with digestive health. Users of prebiotic supplements are highly likely to recognize the more broad-ranging benefits of prebiotics such as enhanced immunity or antioxidant properties. Prebiotics are associated more with digestive health, while fibers are mostly associated with bowel function, though many prebiotics are fibers. Supplementing the diet with easily digestible ingredients such as **inavea™ PURE ACACIA and inavea™ BAOBAB + ACACIA** have shown a proven prebiotic effect for flora balance and gut comfort.

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1. Nutritional + Health Benefits of a Fiber-Rich Diet

Nutrition, Fibers and General Well-Being

The World Health Organization [WHO] asserts that dietary fiber intake should be 25-30g/day for a healthy lifestyle. A 2008 study showed that mean daily dietary fiber intake was 15.9g/day[6]. The advantages of a diet rich in fiber relates to the digestive process and a healthier intestinal tract. A healthy digestive system is characterized by its ability to efficiently process nutrients, to properly nourish the entire organism. Some fibers are rapidly fermented and are associated with high gas production[7] inducing undesirable effects such as abdominal cramps, flatulence, and diarrhea, which can be highly debilitating, impacting overall well-being and quality of life. People who suffer from an unhealthy digestive tract frequently experience these symptoms, as well as other uncomfortable conditions on the other end of the spectrum such as bloating and constipation. Nutritionists recommend a high fiber diet to provide a sufficient dose of fiber without side effects, with the goal of reaching improved digestive tolerance. Healthy food producers want to offer high fiber products that increase satiety sensation, but do not have the adverse side effects that might limit their consumption. High-fiber foods tend to take longer to eat, and they are less "energy dense", which means they have fewer calories for the same volume of food. Fiber consumption can enable additional positive health activities including colonic fermentation stimulation, reduction of cholesterolemia and reduction of postprandial glycaemia [European Commission, Regulation [EU] n°2016/854].

The advantages of a diet rich in fiber are crucial to the digestive process, by shortening the time food passes through the intestinal tract, increasing bulk and stool production, and preventing constipation. Fiber increases the sensation of satiety, reducing calorie intake, which may help with weight management. Soluble dietary fibers may enable additional benefits including colonic fermentation stimulation and reduction of cholesterolemia.

Dietary Fiber: Soluble and Insoluble Fibers

Functional fibers are non-digestible, isolated glycosides that promote physiological benefits in humans. Dietary fibers could also be defined as plant and animal polysaccharides that resist enzymatic degradation in the digestive tract of humans. Fibers are divided in two groups:

- **Soluble fibers that dissolve in water, and are fermented or partially fermented by the gut microbiota**
- **Insoluble fibers that do not dissolve in water but can absorb it**

2. Nexira's inavea™ Range of Ingredients

The **inavea™** range of ingredients provides prebiotic effects for flora balance and gut comfort.
Nexira's **inavea™ PURE ACACIA and BAOBAB + ACACIA** are **Carbon Neutral** ingredients.

inavea™ PURE ACACIA is a gentle, **non-digestible organic** ingredient with **high gut comfort** and **tolerance** [up to 30g/day with no discomfort], that can improve the gut barrier. Strong prebiotic properties were demonstrated from 10g/day: Acacia balances the colon's microbial ecosystem, stimulates healthy bacteria, and activates the production of beneficial metabolites from microbiota. Two in vitro studies[32,33] have demonstrated SCFA synthesis is higher with prebiotic acacia compared to control and FOS, and CMC and Psyllium. The beneficial effects of SCFA production include colon acidification [healthy bacteria selection], improvement of intestinal mobility and the absorption of water and salts, while providing energy to the intestinal epithelium, and improving energy metabolism.

inavea™ BAOBAB + ACACIA selectively boosts the microflora, promoting the growth of beneficial bacteria at **5g/day**, which is two times lower than baobab or acacia alone. With its synergistic prebiotic effects, resulting in SCFA production and antioxidant activities, BAOBAB + ACACIA enables modulation of oxidative and inflammatory markers, maintaining digestive health.

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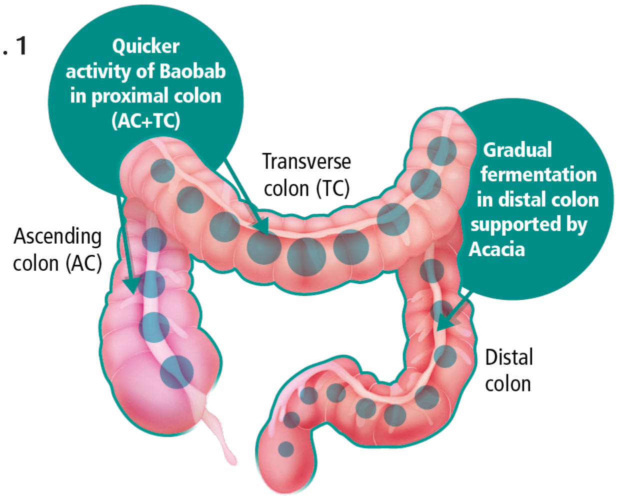
3. The Comfortable Digestibility of inavea™ PURE ACACIA

Acacia is an all-natural, GMO-free source of soluble dietary fiber, carefully obtained from selected gum exudate from the stems and branches of Acacia trees. It provides a guaranteed minimum of **90% soluble dietary fiber** on a dry weight basis [AOAC 985.29 method], 2 to 4% of protein and a few minerals. This arabinogalactan fiber also contains rhamnose and glucuronic acid moiety. The polysaccharide pattern is very specific with notable ArabinoGalactanProteins [AGP] which also provide emulsifying properties to GA. The structure is highly ramified [with specific conformations] and molecular weight is approximately 500 kDa, and can go up to 1 – 5 MDa. This specific structure brings high stability of the polysaccharide to heat or acidic pH, but also a high digestive tolerability as it is slowly fermented throughout the colon.

FODMAP-friendly Certified

IBS affects 70 million people daily, between 10% to 15% of the population worldwide, characterized by abdominal pain or discomfort, and altered bowel habits. Many IBS sufferers turn to a low FODMAP diet in order to limit their digestive issues. **inavea™ PURE ACACIA** and **BAOBAB + ACACIA** are all-natural, **FODMAP-friendly** ingredients. Suitable for a low FODMAP diet, they are gradually fermented in the colon without generating discomfort. inavea™ PURE ACACIA offers fiber enrichment with high digestive tolerance and prebiotic properties at 10g/day. inavea™ BAOBAB + ACACIA has proven prebiotic effects at 5g/day which contribute to the balance of microflora for enhanced digestive health.

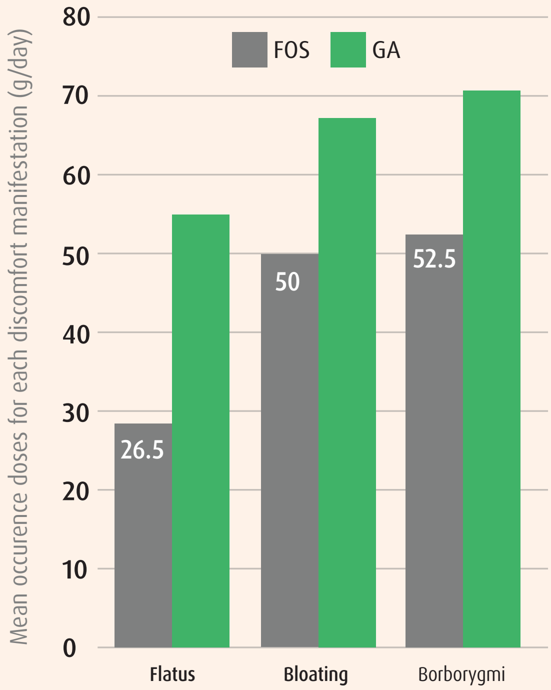
Fig. 1



Multiple studies in the past 40 years have demonstrated the benefits of Acacia on the digestive tract.

Higher digestive comfort compared to FOS

Fig. 2



P<0.05

1. Cherbut *et al.*, 2003 – clinical evaluation 2. Goetze, 2008

Cherbut et al. [2003]: Intestinal Tolerance of Acacia[8]

The Cherbut et al.[8] study of 2003 compared the intestinal tolerance of acacia to that of sucrose [as a neutral reference] and short-chain fructo-oligosaccharide [FOS], a well-known prebiotic fiber. Even when consumed at high doses, adverse gastrointestinal effect of acacia was lower than FOS, and demonstrated a bifidogenic activity; it did not induce flatulence below a dose of 30 g/day, and doses higher than 50 g/day did not provoke abdominal cramps or diarrhea. Thus the high digestive tolerance of acacia was confirmed, with a daily dose of 10g shown to stimulate the growth of *Lactobacilli* and *Bifidobacteria*. **[See Fig. 2]**.

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Goetze et al. [2008]: Acacia Decreases FOS Side Effects[9]

In 2008 Goetze et al.[9] conducted an experiment to assess how partial replacement of FOS by acacia may reduce side effects. The effects of FOS were compared to those of a blend of 50% FOS and 50% acacia. It was shown that FOS generates more abdominal side effects than acacia. Though FOS and the blend both increased the scores for bloating and gas production, there was a tendency of increased scores for belching and 'general' impairment under FOS consumption only, and Borborygmi significantly increased with FOS consumption. Blend showed a slightly lower side-effect profile in comparison with FOS which supports the difference in the digestive comfort of FOS compared to acacia; the addition of acacia to FOS minimized side effects.

Terpend et al. [2013]: Progressive Fermentation of Acacia[10]

To further understand acacia's intestinal tolerance, Nexira conducted an in vitro experiment[10] which helps to further understand the intestinal tolerance of acacia. SHIME® technology, which mimics the human gastro-intestinal digestive tract, was used to compare the digestibility of acacia with that of FOS. Acacia was fermented in the transverse colon with a residual part still available for gradual fermentation in the distal colon. **[See Fig. 4]**. An adaptation of the metabolism of bacteria increased their capability in fermenting acacia during the three weeks of the experiment, which is in compliance with what Angelakis and colleagues[11] [2012] described for high- and low-fiber diets. A short-term measurement [up to 48 h] of gas production confirmed the fast fermentation of FOS, compared to acacia with its gradual fermentation in the distal colon.

Fig. 3

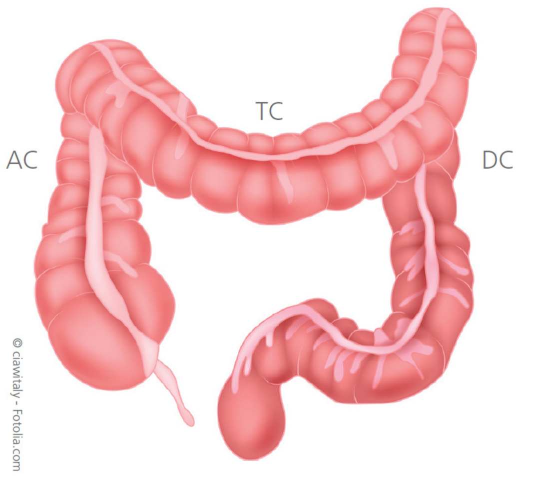
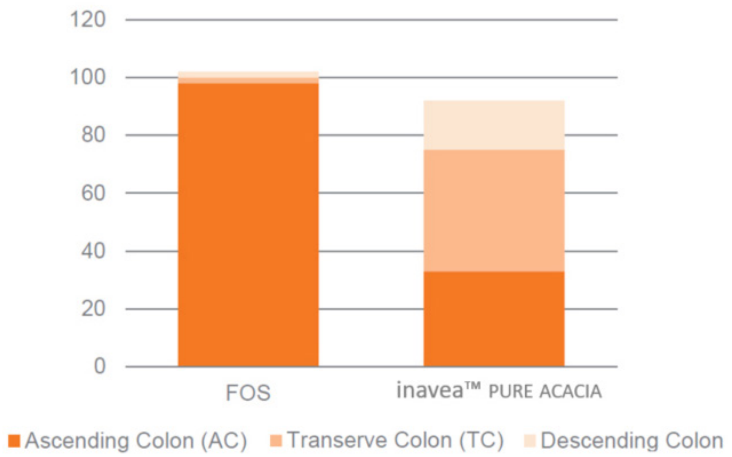


Fig. 4: Comparative fermentation in AT, TC and DC for FOS vs. inavea™ PURE ACACIA



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.

4. Prebiotic Effects of inavea™

The prebiotic effects of Acacia have been demonstrated for 4 decades in more than 40 studies. The clinical study of 2013 on the **progressive fermentation of acacia**[10] demonstrated that **acacia stimulates the growth of *Lactobacilli* and *Bifidobacteria*. [See Fig. 5]**. Prebiotics are defined by ISAP as a substrate that is selectively utilized by host microorganisms conferring a health benefit. *Lactobacilli* and *Bifidobacteria* are indicators of prebiotic stimulation with *Bifidobacteria* being the most significant organisms for gut health.[3] Soluble dietary fiber stimulates colonic fermentation and thus the production of **Short Chain Fatty Acids (SCFAs)**, such as propionate, butyrate and acetate, that can have many potential benefits on the digestive tract, metabolic health, cardiovascular health and immunity.[4] 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, diversity index of bacterial strains, and a decrease in intestinal pathogens.[5] A recent proprietary study by Nexira[31] used a Triple **SHIME**® [Simulator of Human Intestinal Microbial Ecosystem] to compare the prebiotic potential of Baobab fiber with Acacia, and with the combination [Baobab + Acacia], on the composition and metabolic activity of the gut microbiota. The synergies and significant prebiotic activities demonstrated in this study include increased SCFA production, a decrease of ammonium, and an increase of lactate, indicating lactic acid bacteria growth and lower pH, which favors the growth of beneficial bacteria.

inavea™ BAOBAB + ACACIA showed these proven synergistic prebiotic effects on digestive health, using a daily dose of 5g [two times lower than baobab or acacia alone].

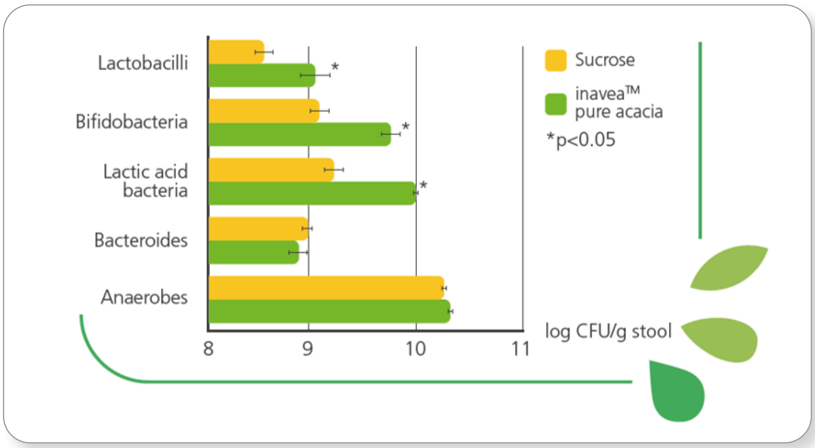


Fig. 5:
Clinical study on healthy volunteers. Increase of LAB with Acacia (10 g/d) compared to control (10 g/d)

Long-Term SHIME® Experiment to Compare the Prebiotic Potential of Baobab Fiber with Acacia, and with the Combination [Baobab + Acacia]

The aim of this project was to **compare the prebiotic potential of Baobab fiber with Acacia, and with the combination [Baobab + Acacia] on the composition and metabolic activity of the gut microbiota** making use of the SHIME® technology platform and considering the potential inter-individual variability in microbiome composition among human individuals.

Materials and Methods

Donor Pre-Screening: The short-term fecal-batch fermentations consisted of a colonic incubation of a representative dose of the test products under simulated conditions of the proximal large intestine. Two doses were tested per product [baobab fiber, acacia, and a combination of baobab fiber/acacia]. Incubations were performed for 48 hours, in fully independent reactors with sufficiently high volume in order to ensure robust microbial fermentation, and to allow the collection of multiple samples over time.

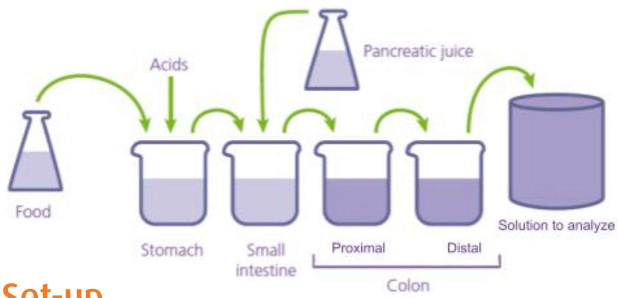
Design of the Long-Term SHIME® Experiment

Typical SHIME® Reactor Set-up: The typical reactor set-up of the SHIME®, representing the gastrointestinal tract of the adult human, was described by Molly *et al.*[34] [1993], consisting of a succession of five reactors simulating the different parts of the human gastrointestinal tract. Upon inoculation with fecal microbiota, these reactors simulate the ascending, transverse, and descending colon.

Adapted SHIME® Set-up for this Study:

To optimally address the research questions, this SHIME® setup was adapted from a TWINSHIME® configuration to a TripleSHIME® configuration, allowing comparison of three different conditions in parallel. Specifically, the properties of the three different test ingredients were evaluated in a TripleSHIME® configuration using the microbiota of a healthy adult human donor.

Fig. 6: SHIME MODEL

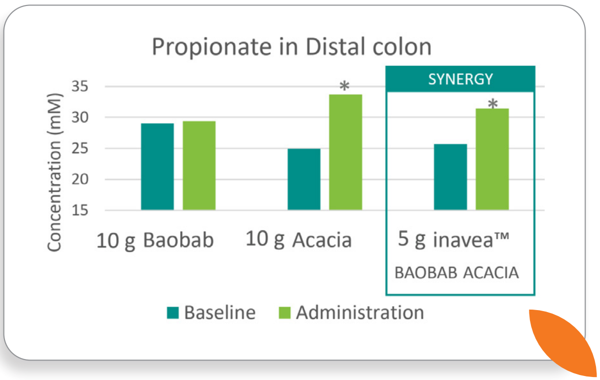


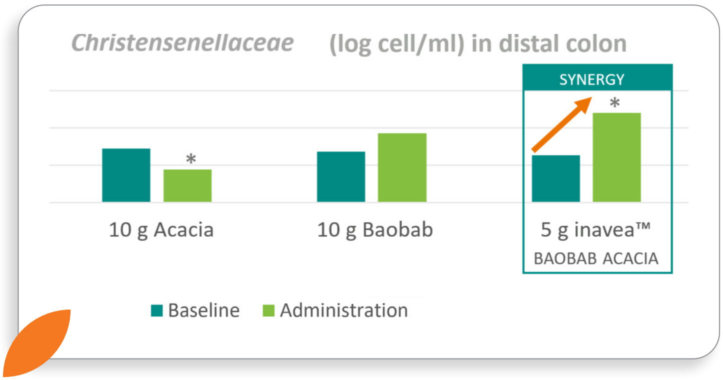
Stability and Reproducibility of the SHIME® Set-up

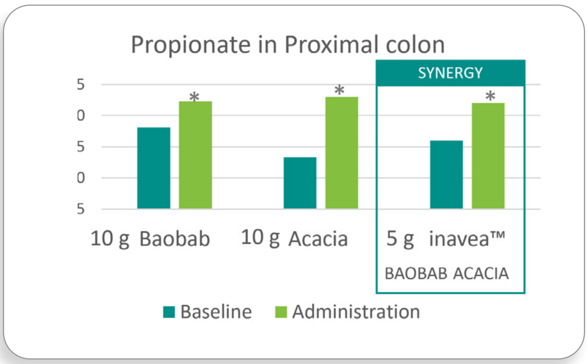
The high stability and reproducibility of the SHIME® Set-up guarantees that any effects observed during the treatment truly result from the administered test products, while the high reproducibility between each of the units allows the direct comparison between the products on virtually identical microbial communities.

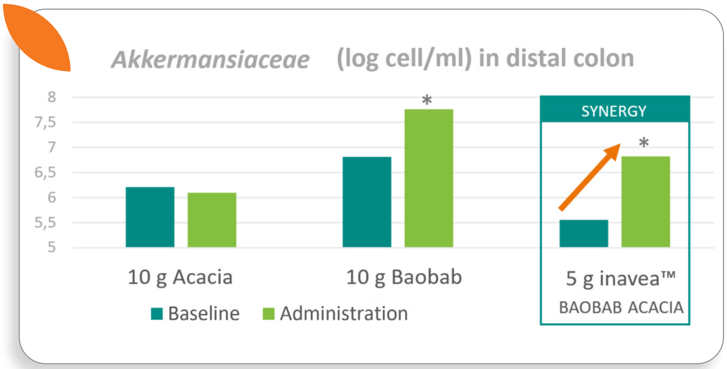
Conclusions of the Long-Term SHIME® Experiment

This experiment has demonstrated the innovative physiological properties of the synergistic formulation, with multiple benefits including an increase in healthy bacteria and SCFA production.[31] This study compared the prebiotic potential of Baobab fiber, with Acacia and with the combination [Baobab + Acacia] on the composition and metabolic activity of the gut microbiota. The donor was selected upon performing short-term colonic incubations with an administration of **baobab fiber, acacia**, and a **combination of both fibers** [tested at two different concentrations] versus a negative control for three different donors. The goal of these colonic incubations was to assess the effects of the test ingredients on overall microbial fermentation [pH] and **microbial metabolic activity** [SCFA, lactate, and ammonium production]. With respect to microbial community structure, only Acacia tended to increase microbial diversity in the AC, while in the TC/DC, a significant increase in diversity was observed upon supplementation of Baobab fiber and Acacia. With respect to exact microbial changes, an administration of Baobab fiber significantly stimulated an OTU [Operational Taxonomic Unit] related to Bifidobacterium adolescentis, while an administration of Acacia specifically enhanced an OTU related to Bifidobacterium longum. Administration of **Baobab fiber in its combination with Acacia** significantly increased overall Bifidobacteriaceae levels. The combinatory product resulted in enhanced levels of Ruminococcaceae, Eubacteriacea, and Christensenellaceae in TC/DC. Finally, there was a reduction of several families within the Proteobacteria phylum in the AC, a phylum containing multiple opportunistic pathogens.









The main endpoints of the **long-term SHIME® experiment** were related to the effect of the test products on the metabolic activity of the gut microbiota: general markers for fermentation [acidification] and specific markers for saccharolytic fermentation [SCFA, lactate] or proteolysis [ammonium and branched SCFA]; and on the composition of the luminal microbial community by 16S-targeted illumina sequencing. Overall it was concluded that these ingredients have large prebiotic potential.[31]

It has been concluded that **inavea™** BAOBAB + ACACIA has a **proven prebiotic effect with a dose 2 times lower than Baobab or Acacia alone.**

Postbiotics Released During the Fermentation Process

Postbiotics are compounds released by microbiota during fermentation. These metabolites highlight pathways and can provide benefits through interaction with the host. The 2020 study[31] included an extensive screening of more than 500 microbiota metabolites, and demonstrated the properties of **inavea™ BAOBAB + ACACIA**: antioxidant activities, microbiota balance, and modulation of inflammatory markers. The reduction in 5-Aminovalerate, methionine oxidation, and conjugated bile acids, together with an increase in abscisic acid [only upon administration of Baobab fiber], and polyamines indicated beneficial effects for the host.[31]

5. The Effect of the Gut Barrier on Overall Health

The human body is colonized by commensal microorganisms that interact with organs to maintain our natural barriers against external factors. The body consists of two main natural barriers:

- The first line of defense is the skin, which is the largest organ. Here reside several microorganism communities that contribute to immune protection.
- The second barrier is the intestine which is composed of a monolayer of epithelial cells sitting on a specialized extracellular matrix [intestinal wall]. The intestine is colonized by trillions of bacteria [microbiota]. This barrier is involved in both innate and adaptive immune responses and can control the passage of nutrients, water, ions, and macromolecules. The intestinal mucosa is constantly exposed to a vast array of microbes, food antigens and toxins. Gut microbiota enables the tolerance of many antigens.

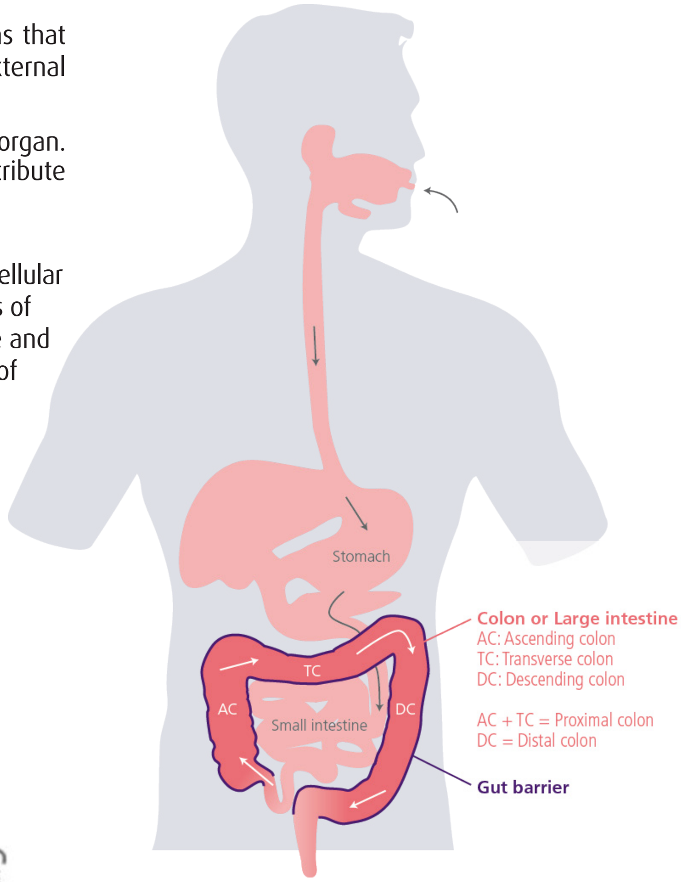


Fig. 7:
Gut Microbiota + Intestinal Wall = Gut Barrier

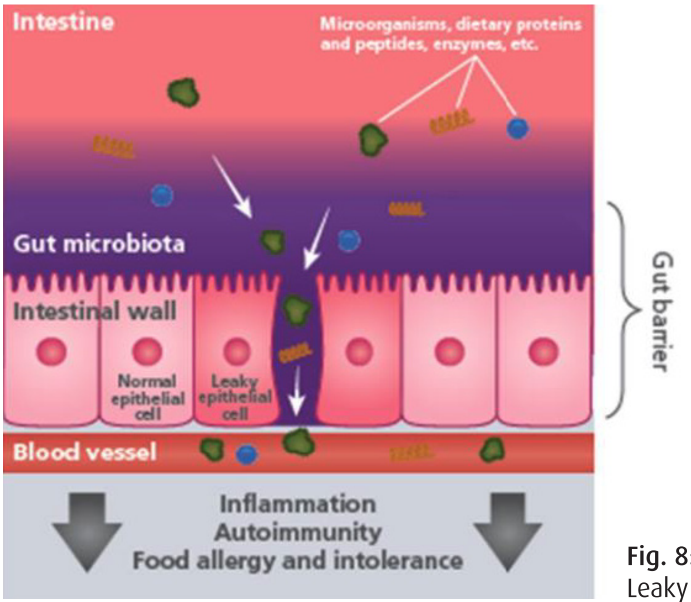


Fig. 8:
Leaky Gut Mechanism

One of the most important roles of the gut barrier is to distinguish between pathogenic and non-pathogenic compounds. Intestinal inflammation compromises the gut barrier and alters gut impermeability, known as Leaky Gut Syndrome **[See Fig. 8]**. With LGS, invasive molecules that are not blocked by the intestinal barrier can penetrate the organism. Maintenance of the gut barrier within is just as important as caring for the outer skin.

Gut Barrier Functions

The gut barrier provides crucial protection against potential allergic reactions and microbiological threats. The overall interest in gut health, and specifically in the gut barrier, has grown incrementally, with millions of people worldwide impacted by IBS.[13,14] The incidence of impaired and increased gut permeability, also known as Leaky Gut Syndrome [LGS], is closely studied because of its potential involvement in IBS, as well as other diseases. Modulating the composition and activity of gut microbiota can decrease the risks posed by LGS.

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To understand the effect of Acacia on the intestinal tract, Nexira conducted an *in vitro* experiment on healthy donors. This study[10] performed with the SHIME® technology demonstrated the specific and progressive gut fermentation of acacia versus fructooligosaccharides [FOS]. This study, as well as the clinical trial performed by Cherbut *et al.*[8], [2003], confirmed the prebiotic performance of acacia. Based on the positive results obtained by those previous studies, Nexira conducted further ambitious experiments to demonstrate the innovative physiological properties of acacia on gut permeability. FOS was again used as the comparative reference and the results matched the previous experiments.

IBS Subjects

The causes of IBS and its subsequent development involves intestinal hyper-permeability, inflammation, and the incidence of specific microbiota. This is why patient donors with IBS were asked to participate in this study to investigate the loss of intestinal epithelial barrier function.

SHIME® & M-SHIME® Experiments

SHIME®, used in experiments to mimic the gastrointestinal tract [GIT], simulates the stomach, small intestine and the three regions of the large intestine [ascending, transverse, descending]. Plastic beads covered with a layer of mucin agar can be added to each of the compartments simulating the colon[24], mimicking the processes that occur in the GIT, thereby allowing investigation of luminal and mucus associated microbial communities.

Acacia has been shown to increase the intestinal population of Bifidobacteria and Bacteroidetes, known to be commensal healthy bacteria, and more specifically the anti-inflammatory bacterium, *Faecalibacterium prausnitzii.*[25] The prebiotic effect of dietary fiber increases the growth of specific bacteria that have important physiological and health benefits for the host.

Studies on luminal microbial communities that do not adhere to intestinal mucosa using SHIME®:

- In studies with IBS patient donors, acacia has been shown to slightly increase total bacteria populations in each of the colon compartments of the SHIME® device.

Studies on mucosal microbial communities that adhere to/interact with intestinal mucosa using M-SHIME®:

- *Roseburia* bacteria, which produces beneficial the SCFA butyrate, increased in the proximal colon.
- The mucosa-associated and anti-inflammatory bacteria Faecalibacterium prausnitzii population is increased in the proximal and distal colon compared to the control.

Prebiotic dietary fibers have been shown to positively affect the intestinal bacteria responsible for beneficial SCFA production in IBS sufferers.

Under lipopolysaccharides [LPS] stimulation, experiments on pro-inflammatory cytokines involving IBS patient donors indicate that acacia completely inhibited NF-kB/ AP1 activity by the end of treatment. For TNF-B the trend was more fluctuating, and IL-8 secretion was mildly reduced. In a complementary way, the anti-inflammatory cytokine IL-10 was increased by acacia. Regarding the pro-inflammatory cytokines, acacia produced the strongest decrease in NF-kB/ AP-1 activity in the proximal and distal colon. Secretion of IL-8 and IL-6 were reduced in both the proximal and distal colon. IL-10 was increased in the distal colon. These results demonstrate that the modulation of inflammatory markers by acacia is based on two actions: inhibition of pro-inflammatory cytokines and stimulation of anti-inflammatory ones. [See Table 1 for values].

Table 1:
Modulation Assessed at Conclusion of Experiment

IBS	Ascending Colon	Transverse Colon	Descending Colon
NF-kB/AP1		-100%	-100%
TNF alpha	-62%	+29%	-40%
IL-8		-85%	-31%
IL-10	Induction	Slight decrease	

IBD	Proximal Colon	Distal Colon
NF-kB/AP1	-16%	-24%
TNF alpha	No induction or reduction	
IL-8	-12%	
IL-6	-32%	
IL-10	+32%	

Pro-inflammatory cytokines
Anti-inflammatory cytokines

Intestinal Gut Permeability Modulation

Samples collected during the 2015 studies were used in a cell line model to assess potential gut wall modulation, specifically impermeability. Acacia demonstrated a protective effect on barrier integrity as shown by an enhanced cell impermeability.[26, 27]

Reinforcement of the Gut Barrier at the Cellular Level

As in previous experiments, acacia has been shown to increase the intestinal population of the commensal healthy bacteria. Prebiotic ingredients have been shown to induce an increase in total SCFA production and exert a butyrogenic effect in the distal colon. These results support the conclusion that the distal colon is the main area of bacterial fermentation of acacia fiber. Under lipopolysaccharides [LPS] stimulation, experiments indicated that acacia's modulation of inflammatory markers is based on two combined actions: the inhibition of pro-inflammatory cytokines and, in a complementary way, the stimulation of anti-inflammatory cytokines.[25]
In 2016, Nexira worked with the INSERM [Institut National de la Santé Et de la Recherche Médicale] to carry out further experiments. This recognized scientific organization, the French National Institute, specializes in health and medical research. These studies were dedicated to research the mechanisms of the gut impermeability restoration at a cellular level.

Tight Junctions

Tight junctions are different types of proteins: Claudin-1, Zonula Occludens [ZO-1] and Occludin.

- They consolidate the paracellular barrier that controls the flow of molecules in the intercellular space between the epithelium cells.
- They are the closely associated areas of two cells whose membranes join forming a virtually impermeable barrier to fluid.
- Tight junctions are widely studied for their implication in the gut permeability in the IBD[29] and for the involvement of the gut microbiota in their permeability.[30]

Fig. 9: Tight Junctions

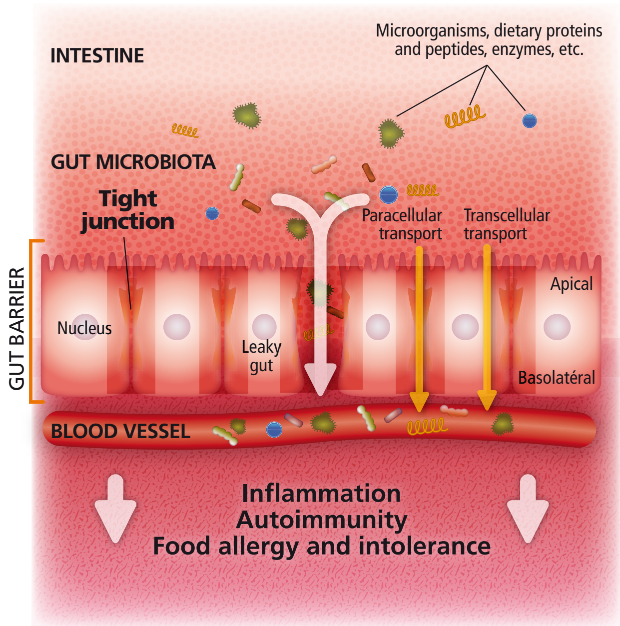
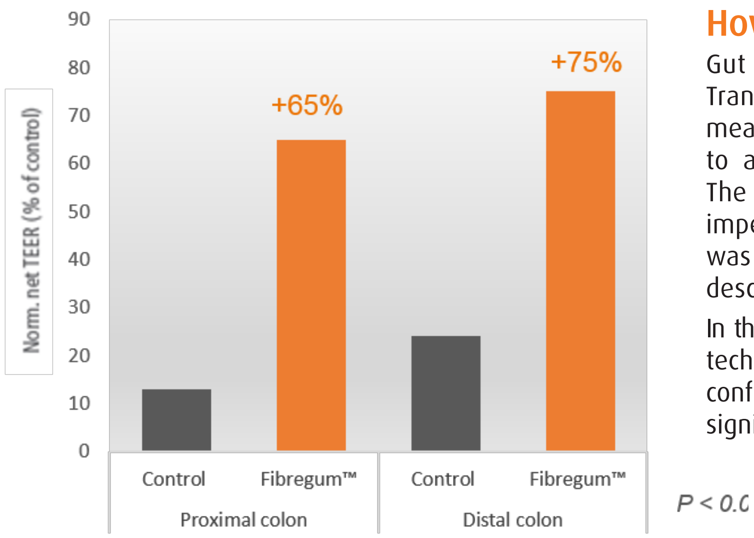


Fig. 10: TEER



How Gut Permeability is Assessed

Gut permeability is assessed by the utilization of Trans Epithelial Electrical Resistance (TEER), which measures electrical resistance through a membrane to assess the global quantitative impermeability. The higher the resistance, the more the cell line is impermeable. During a previous experiment, TEER was used to sample fermentation products on the descending part of the artificial colon.

In the subsequent experiment using two complementary technologies, TEER and FITC-dextran, it has been confirmed by both technologies that these samples significantly reduce the cell line permeability.

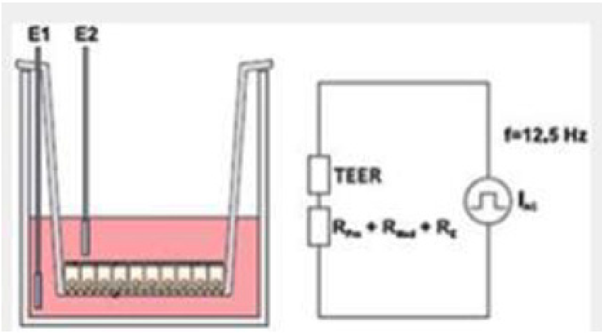


Fig. 11

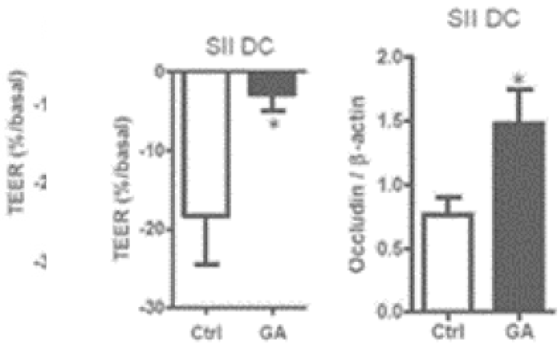


Fig. 12

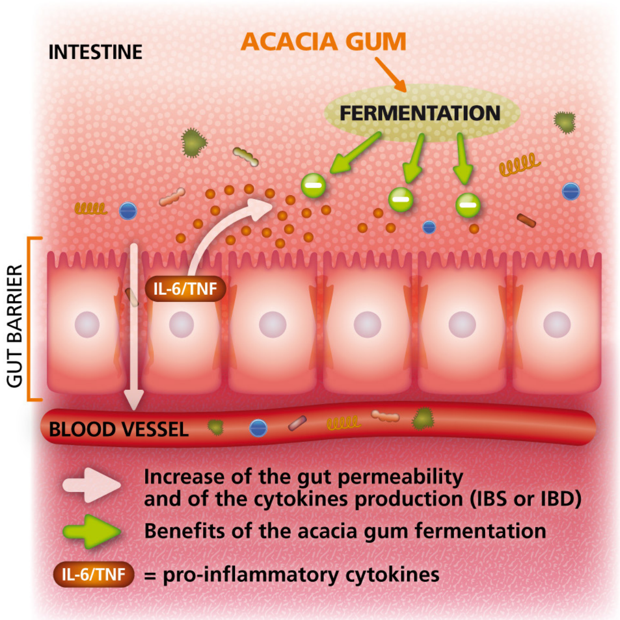
Effects of Acacia on Gut Permeability on IBS Subjects

During this study, activity at the tight junction level was assessed with the protein expression. The Claudin-1 and ZO-1 revealed a trend of increase, and the Occludin increased. Furthermore, an increase of the ARM coding for Occludin was measured; the number of Occludin tight junctions increased, improving the gut impermeability.

Effects of Acacia on the Inflammatory Response on IBS Subjects

The modulation of inflammatory markers by acacia fermentation has been tested both on the apical and basolateral sites of the cells. The cytokines concentration at the basolateral level were too low to be measured. At the apical level, IL-6 and TNFα, two pro-inflammatory cytokines, showed similar profiles. The IL-6 concentration has been reduced in all three parts of the colon, though the TNFα concentration has only decreased in the transverse and descending parts [see table]. The fermentation, occurring in the transverse and descending colon, has a positive effect by reducing the pro-inflammatory cytokines.

Fig. 13



Tight Junctions	Increase (x)	P value
Claudin-1	1.8	NS
ZO-1	2.1	NS
Occludin	1.9	0.0381

NS: Non-Significant

Pro-inflammatory cytokine reduction

	IL-6	TNFα
Ascending colon	0.53 ($p<0.05$)	-
Transverse colon	0.48($p<0.05$)	0.41 ($p<0.05$)
Descending colon	0.55($p<0.05$)	0.53($p<0.05$)

Conclusion

These experiments confirmed that the fermentation of acacia in the distal part of the colon exerts beneficial effects on the improvement of the gut impermeability and inflammation, and provided new information on the mechanism involved at the cell level. It indicates that the acacia fermentation may exert its activity by reinforcing the tight junctions and by modulating inflammatory markers at the apical level of the cells.

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GENERAL CONCLUSION:
inavea™ PURE ACACIA and BAOBAB + ACACIA are Extremely Well-tolerated Prebiotic Ingredients that Promote Gut Health

This technical paper shows the excellent tolerance of **inavea™ PURE ACACIA and inavea™ BAOBAB + ACACIA.** This tolerance is notably due to the slow fermentation of acacia by the gut microbiota. This gradual fermentation and high tolerability make acacia a very powerful tool to increase dietary fiber content, even for people suffering from high digestive discomfort such as IBS.[12] It has confirmed that acacia's fiber is progressively and gently fermented in the intestinal tract[10, 31] and provides well-known SCFAs. When inavea™ BAOBAB + ACACIA was administered, there was an increase in overall levels of healthy bacteria, thereby demonstrating a positive effect on the microbiota. The properties of **inavea™ PURE ACACIA and inavea™ BAOBAB + ACACIA** can help improve intestinal well-being and overall gut health.

inavea™ PURE ACACIA

- Demonstrated prebiotic effect at 10g/day
- Well-tolerated prebiotic acacia: High digestive tolerance with slow fermentation
- FODMAP-friendly / High fiber content
- Provides immunity benefit through restoration of the gut barrier permeability

inavea™ BAOBAB + ACACIA

- Proven synergistic prebiotic effect at 5g/day [2 times lower than Pure Acacia or Baobab alone]
- Full Spectrum gut fermentation and gut comfort
- FODMAP-friendly
- Provides Microflora balance

To summarize, **inavea™ PURE ACACIA and inavea™ BAOBAB + ACACIA** present powerful health benefits associated with a high digestive comfort that will allow consumption by a wider range of consumers.

TABLE OF ABBREVIATIONS

IBS: Irritable Bowel Syndrome
IBD: Inflammatory Bowel Disease
LGS: Leaky Gut Syndrome
CFS: Chronic Fatigue Syndrome
SCFA: Short Chain Fatty Acid
LPS: lipopolysaccharides
INSERM: Institut National de la Santé Et de la Recherche Médicale
FODMAPs: Fermentable oligo, di- and monosaccharides and polyols
TEER: Trans Epithelial Electrical Resistance
FITC: Fluorescein Isothiocyanate
OTU: Operational Taxonomic Unit

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