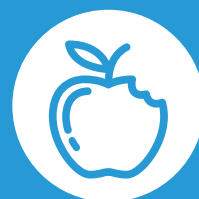




Litesse[®]



The sustained prebiotic for digestive health

Litesse[®] polydextrose, part of IFF's ingredient range, is well established as a specialty carbohydrate for a variety of food applications. It is widely used as a fiber as well as a premium bulking ingredient for sugar and fat replacement. It helps reduce calories, sugar and lowers glycemic load while improving flavor, mouthfeel and fiber content.

Litesse[®] can also provide benefits to digestive health. A number of human, animal and *in vitro* studies provide the scientific support for Litesse[®] as an effective prebiotic.

STUDIES SHOW THAT LITESSE[®]

- ✓ Is not hydrolyzed by digestive enzymes and passes intact to the colon^{1,2}.
- ✓ Is fermented slowly and consistently throughout the colon, thus mediating its effect also in the distal colon where disease risk may be greatest^{1,2}.

Product category |

DIGESTIVE & METABOLIC



PRODUCT ATTRIBUTES

- Dietary fiber
- Prebiotic properties
- Provides just 1 kcal/g
- Low glycemic ingredient
- Outstanding toleration
- Superior functionality for sugar reduction

- ✓ Enhances saccharolytic (carbohydrate) fermentation, thus reducing colonic pH^{3,4}.
- ✓ Selectively stimulates the growth of bifidobacteria and lactobacilli^{3,5}.
- ✓ Enhances immune response, especially in combination with lactitol, where a synergistic effect occurs⁴.
- ✓ Promotes the generation of short chain fatty acids including acetic, propionic and butyric, of which the latter two have specific documented health benefits⁶.
- ✓ Improves colonic mucosal integrity by reducing cox-2 expression⁶.
- ✓ Can optimize calcium absorption and bone retention in an ovariectomized rat model^{7,8}.

LITESSE® AS A SUSTAINED PREBIOTIC

Litesse® is a highly branched polymer of glucose. Its unique arrangement of glycosidic linkages makes it resistant to hydrolysis by human digestive enzymes. After ingestion it passes intact into the colon where it is partially fermented by the colonic microbiota. In this way Litesse® contributes an energy value of just one calorie per gram. It is the preferred specialty carbohydrate for a wide variety of processed food applications including baked goods, confectionery, dairy products and beverages. Human studies^{3,5,9}, combined with *in vitro*² and animal data¹, demonstrate that Litesse® functions particularly well as a prebiotic, sustaining its impact throughout the colon. This prebiotic activity provides food formulators with a new option for innovative products targeted at digestive health.

This monograph provides a brief introduction to prebiotics and summarizes the data that demonstrates Litesse® is an effective prebiotic.

DIGESTIVE DISORDERS AND NUTRITIONAL STRATEGIES

Digestive disorders represent a major public health issue. Between 10 and 20% of the population of industrialized countries experience a range of digestive symptoms including diarrhea, constipation, irritable bowel syndrome (IBS), ulcerative colitis, Crohn's disease and cancers, with colon cancer being the most prevalent of the digestive tract cancers.

As an example, the following statistics have been published for the USA¹⁰ and the situation is quite similar in other countries.

STATISTICS ON DIGESTIVE DISORDERS:

- ✓ **Prevalence:** 60 – 70 million people affected
- ✓ **Mortality:** 245,921 including deaths from cancer
- ✓ **Hospitalizations:** 21.7 million people
- ✓ **Diagnostic and therapeutic procedures:** 5.4 million people (12% of all procedures)
- ✓ **Costs:** 142 billion dollars of which - 98 billion dollars are direct medical costs - 44 billion dollars are indirect costs (disability and mortality)

Diet and lifestyle are generally accepted as playing major roles in mediating digestive disorders. Reducing risk via nutritional strategies is an important objective.

FIBERS, PROBIOTICS AND PREBIOTICS

Food manufacturers have several ways of facilitating improved digestive health. These opportunities include probiotics, prebiotics, synbiotics and fiber.

According to ISAPP (International Scientific Association for Probiotics and Prebiotics):

A probiotic is a live microorganism which when administered in adequate amounts confer a health benefit on the host. Probiotics are a well-established market, via dairy products such as yogurts, and are also available to consumers as convenient individual doses in beverage and dietary supplement form.

A prebiotic is a substrate that is selectively utilized by host microorganisms conferring a health benefit.

A synbiotic is a mixture comprising live microorganisms and substrate(s), pro- and prebiotics, selectively utilized by host microorganisms that confers a health benefit on the host.

Fiber can be defined in many ways. Physiologically, fiber is essential to maintain regular bowel function and it also has glucose and/or cholesterol attenuating effects. Fibers are also an important source of food for some beneficial gut bacteria. Comprehensive reviews on fiber and health are available^{11,12}.

Litesse® is recognized as an important fiber source in many countries worldwide. Unlike other prebiotic fibers, Litesse® is extremely well tolerated due to its slow fermentation and thus is less likely to cause gastric discomfort¹³. The positive effects of Litesse® as a sustained prebiotic fiber are apparent at doses as low as 4 grams per day in humans.

FIBER PROPERTIES OF LITESSE®

The main difference between a prebiotic and a fiber is that a prebiotic specifically mediates its effect via the gut microbiota whereas a fiber may or may not influence the microbiota. Beneficial physiological effects of fibers include fermentation, laxative effect and attenuation of blood cholesterol level and glucose response¹². Polydextrose has been shown to cause beneficial gastrointestinal effects and thus fulfill the definition of dietary fiber^{3,9;14,15,16,17,18,21}. Polydextrose has been shown to have beneficial effects on lipid metabolism by increasing HDL²² and reducing postprandial glycemia^{3,23} as well as triglyceride responses^{24,25}.

Dietary fibers are also known to contribute to weight management. Recent human studies have shown that Litesse® polydextrose contributes to satiety and reduced energy intake^{26,27,28}. Meta-analyses and systematic reviews on Litesse®^{19, 20} have shown that the consumption of Litesse® reduces voluntary energy intake at a subsequent meal. Furthermore, this reduction in energy intake occurs in a dose-dependent manner¹⁹. Litesse® polydextrose reduces the desire to eat during the satiation period²⁰. This may explain, at least in part, the observed effects of polydextrose on the reduction of levels of energy intake at subsequent meals.

PREBIOTICS AND HEALTH BENEFITS

The average adult digestive tract contains about 0.2 kilogram of bacteria, most of which are present in the colon. There are about as many bacterial cells in our body as we have human cells²⁹.

Over 1000 species have been identified³⁰ and it is believed that there are many more as yet unidentified. The metabolic activity of bacteria in the colon is similar to that in the liver, our most active organ. These bacteria have a major influence on our health and wellbeing. Most are beneficial but some are potentially harmful. A majority of the microbes in our intestines have not been characterized and their specific influence on our health is unknown. A good balance is essential for optimal gut health. Saccharolytic (carbohydrate fermenting) bacteria such as lactobacilli are considered to be desirable and enhancing their prevalence in the colon has become a major objective of digestive health strategies.

Figure 1 summarizes the possible impact of a prebiotic on the intestinal microflora.

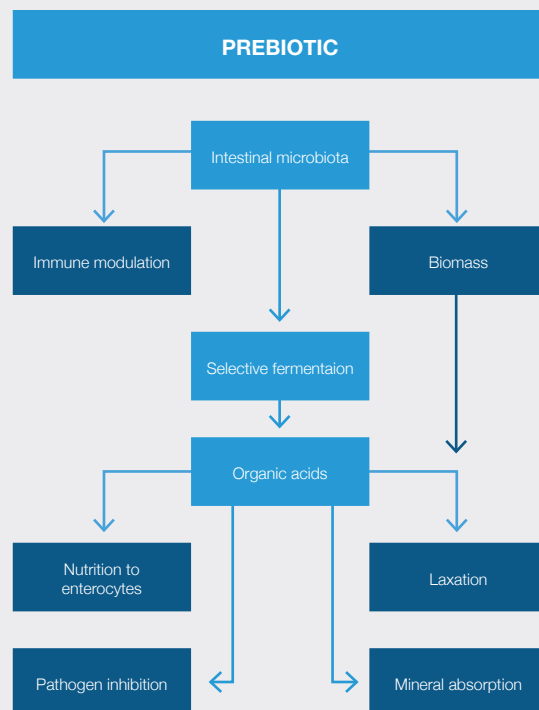


Figure 1 summarizes the possible impact of a prebiotic on the intestinal microflora.

TREATMENT	Cultured bifidobacteria log ₁₀ colony forming units/g faeces
Control/Run-in	7.0 +/-2.2
Probiotic mixture	7.6 +/-2.0
Probiotic mixture with Litesse®	8.9 +/-2.5 ***
Washout	8.5 ± 1.5*

Table 1 stimulation of fecal bifidobacteria by Litesse® (5g/day) in 20 subjects after two-week period consumption of probiotic mixture (*Bifidobacterium breve* BBi, *L. rhamnosus* LC705, *Lactobacillus* GG and *Propionibacterium freudenreichii* ssp. *Shermanii* JS, 2x 10¹⁰ viable bacteria/day), probiotic mixture with Litesse® and after washout period⁹.

By increasing the number or the activity of the beneficial bacteria with prebiotics, the harmful bacteria may be suppressed. Changing this balance of beneficial and harmful microbes has been shown to have a positive influence on the health of the consumer. More specifically, the change in microbiota composition may lead to an improved or changed immunological status. Furthermore, selective fermentation will lead to the formation of short chain organic acids, which exhibit a wide spectrum of biological activity. Short chain organic acids provide an important energy source for the intestinal epithelial cells, can inhibit (potential) pathogens, may influence mineral absorption and can have a laxative effect, by a bulking effect of the stool (Table 1).

EFFECTS OF LITESSE[®] ON COLON MICROBIAL COMMUNITY STRUCTURE AND ACTIVITY

Litesse[®] has been shown to exert several positive prebiotic effects. Firstly, ingestion of Litesse[®] increases the numbers of bifidobacteria and/or lactobacilli, as has been shown in two independent clinical trials (Table I, Figures 2, 3, 4 and 5).

In addition to the clinical studies, colon simulation work done in collaboration with Professor Glenn Gibson at the University of Reading³¹ confirms the stimulation of bifidobacteria at each stage of colonic fermentation (Figure 6). Importantly, the numbers of true clostridia were not increased by the availability of Litesse[®] for colon microbes. This is noteworthy since these bacteria, although part of our normal microbiota, can in certain conditions be harmful and cause disease. Litesse[®] was the most effective prebiotic in the distal colon where the risk for some diseases is the greatest. In this part of the colon, carbohydrates are often in short supply for the intestinal microbiota. The microbiota will then turn to proteins as an energy source, this leads to the formation of potentially toxic substances such as biogenic amines, ammonia, indole etc. Hence the persistence of a prebiotic into the distal colon will stimulate saccharolytic fermentation there and reduce the formation of toxic substances from protein breakdown.

The reduction of pH in the intestinal tract further inhibits pathogens. Ingestion of Litesse[®] has been shown to decrease intestinal pH in both an animal study⁴) and in a human intervention study³. The reduction of pH may be explained by increased production of short chain fatty acids (SCFA) and inhibition of putrefactive protein fermentation. Enhanced production of SCFA has been demonstrated both *in vitro*^{31,32} and *in vivo*³. A sustained availability

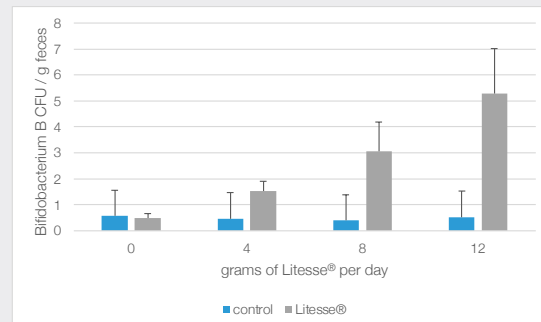


Figure 2

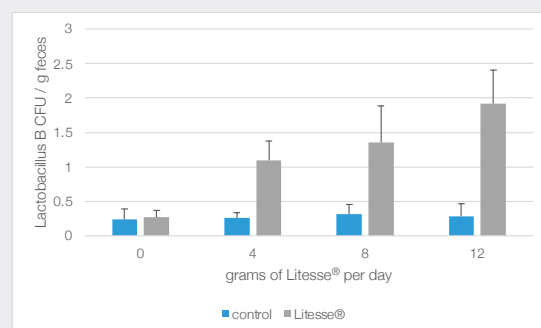


Figure 3

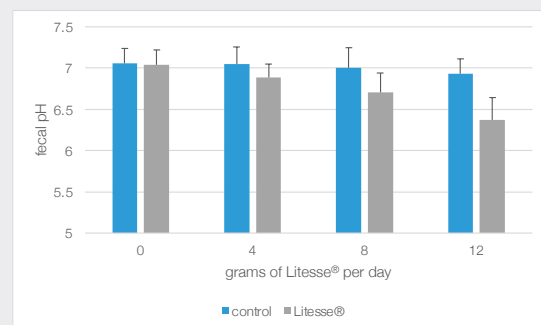


Figure 4

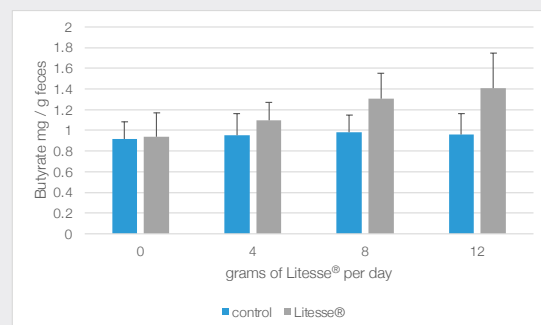


Figure 5

Figure 2,3,4 and 5 enhanced growth of bifidobacteria, lactobacilli and reduced pH and production of butyrate in fecal samples from a clinical study with 120 healthy subjects ingesting 0, 4, 8 or 12 grams of Litesse[®] daily for four weeks (adapted from Jie et al.,2000³).

and fermentation of Litesse[®] starting from the proximal site and continuing to the distal colon site has also been observed with a three-stage colon fermentation model (Figure 6 shows the results from Probert *et al*³¹).

EFFECTS OF LITESSE ON MUCOSAL INTEGRITY

Fermentation of Litesse[®] has beneficial effects on mucosal function. Enhanced butyrate production serves as an important energy source, not only for epithelial cells, but also for the mucosal immune cells. Stimulation of intestinal IgA antibody production is associated with a well-balanced mucosal immune response and protection against infections. Litesse[®] can increase production of intestinal IgA in the large intestine (Figure 7)⁴. A synergistic effect was seen with lactitol.

Balancing immune responses in the large intestine may play a role in reducing colon cancer risk. A possible mechanism for reduction in cancer development is regulation of mucosal gene expression. Over-expression of cyclooxygenase-2 (cox-2) is related to early stages of colon cancer development and chronic inflammatory diseases in the intestine. When two different *in vitro* systems — a four-stage simulator of colonic fermentation and a cell-culture based model of human intestinal epithelial function — were combined in order to study the effects of Litesse[®] on colon mucosal integrity, a dose-dependent effect on reducing cox-2 expression was observed in Caco-2 cells³². Reduction of cox-2 expression by colonic fermentation of Litesse[®] indicate balanced cox expression and thus improved mucosal integrity. Litesse[®] has also been shown to reduce the number of tumors in an animal model³³. The effect was particularly evident in the rectum, demonstrating the protective effect of Litesse[®] in the distal intestine.

MARKET OPPORTUNITIES FOR LITESSE[®] AS A PREBIOTIC

There is growing interest around the world in targeting digestive health with functional foods. Litesse[®] is a convenient and versatile ingredient which is highly stable and compatible with other food components. It can be formulated into a wide variety of food products with the added benefit of improving digestive health.

Figure 8 shows the high stability of Litesse[®] compared to an alternative commercially available prebiotic.

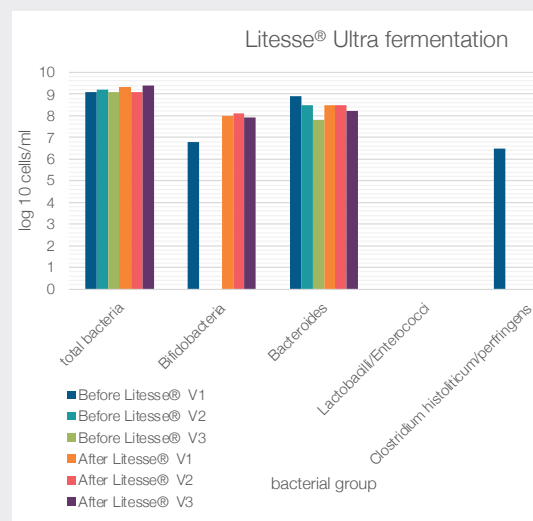


Figure 6 effect of Litesse[®] Ultra on populations of colon microbes in a three-stage *in vitro* simulation (adapted from Probert *et al.*, 2004³¹)

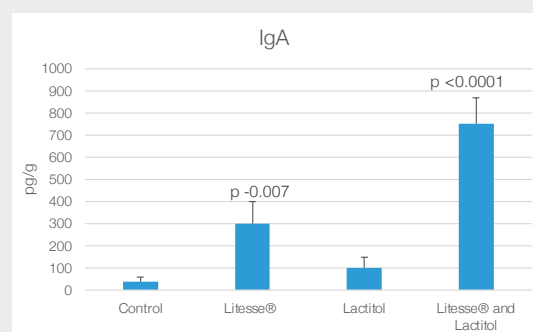


Figure 7 concentration of IgA in the contents of caecum of rats (12 in each group) fed with control; 2% Litesse[®], 2% lactitol or Litesse[®] in combination with lactitol 2% w/w of each component for 3 weeks. (Peurinen, *et al*)

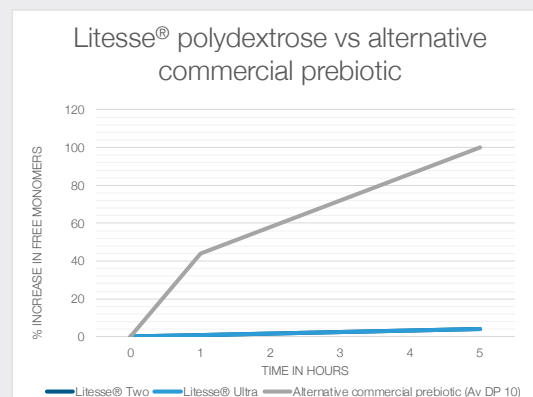


Figure 8 relative stability of 5% w/w solutions of Litesse[®] Two, Litesse[®] Ultra and an alternative commercial prebiotic after heating for 5 hours at 100°C, pH2.6.

Litesse® demonstrates superior stability compared to the alternative prebiotic under test conditions.

Figure 9 shows that Litesse is fermented slowly and consistently throughout the colon².

REGULATORY

Specific prebiotic labeling rules are not yet common. Labeling legislation has not caught up with this recent innovation. Litesse® has been scientifically substantiated as a prebiotic and in some areas, this is adequate justification for a label claim. However, this may not be accepted everywhere. It is important to review finished products with regulatory authorities in order to clarify what can be said on an individual product basis.

Note: All the studies referred to in this review used IFF's premium brands Litesse®, Litesse® Two, or Litesse® Ultra™.

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Please contact your local IFF representative for further details.

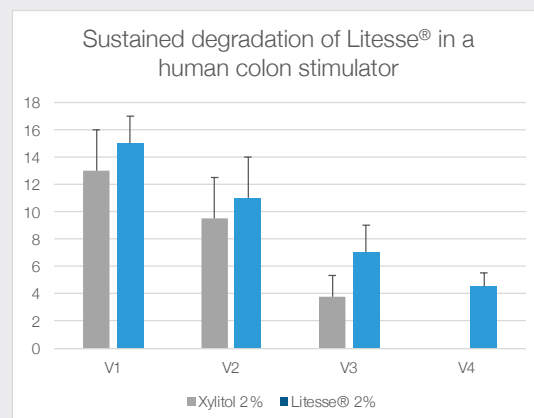


Figure 9 sustained degradation of Litesse® in a in a four-stage *in vitro* human colon simulator

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