Gut Defense

How IgG Binding Protein LT Supports Barrier Integrity Over Conventional Immunoglobulins

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Why gut-health solutions matter: The importance of a balanced microbiota

In the last decade, gut health has rapidly gained importance among consumers and researchers, driven by increased awareness and advancing scientific evidence. Central to this interest is mounting research showing that a balanced gut microbiota supports overall health, while an unbalanced gut microbiota is linked to metabolic, immune, and gastrointestinal (GI) disorders.[1,2] Together with the intestinal barrier, the gut microbiota forms a critical defense system protecting the body against unwanted bacteria.

However, this defense system is sensitive and can easily be disturbed by external factors like antibiotics, poor diet, and unhealthy metabolites, leading to gut dysbiosis.[3] Gut dysbiosis with its reduced microbial diversity, can cause a person to be more susceptible to GI concerns, highlighting the need for solutions that support microbial resilience.[4] This knowledge has led to a variety of gut health solutions that preserve or restore gut health balance, with a particular focus on supporting the gut microbiota's core functions: digestion, metabolism, and immune regulation.

Immunoglobulin-based approaches to gut resilience

Immunoglobulins are essential for the body's immune response and serve as key components supporting gut resilience.[5,6] Maternal immunoglobulins in breast milk exemplify this by providing passive immune support and protecting infants during the critical early period.[7] There are currently various immunoglobulin-containing gut health supplements on the market, including bovine colostrum (BC), serum-derived bovine immunoglobulin isolate (SBI), and immunized egg powder containing the avian immunoglobulin IgY. These products are intended to promote microbial diversity, bind unwanted bacteria, support gut barrier integrity, and modulate local immune responses.[8–10] By promoting the body's natural immune defense, they help maintain a balanced gut microbiota, supporting overall digestive wellness. Although BC is by far the most well-known and studied immunoglobulin supplement, SBI and immunized egg powder have gained attention in recent years for their more concentrated immunoglobulin content and as dairy-free colostrum alternatives.

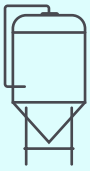
SOURCE	DOSE (mg)	ORIGIN & CONTENT	INGREDIENT INSIGHT
Bovine colostrum			
Bovine 	1000-3000*	The first milk produced after birth, which includes macro- and micronutrients, antimicrobial components, immunoglobulins (IgG, IgA and IgM), and growth factors. It is important for supporing growth, development and immune defense of neonates. [11]	Immunoglobulin content varies significantly depending on the breed, age, feeding of the cow, and timing of collection. [12] Contains milk-allergen & lactose.
SBI			
Bovine 	1000-2000	Serum proteins isolated and concentrated from the blood of cows. Besides immunoglobulins, SBI contains many serum-derived proteins, including transferring and albumin. [9]	The immunoglobulin content in SBI is much higher than colostrum, due to the way it can be concentrated from serum. Ensures consistent protein content. Milk and dairy-free.
Immunized egg powder			
Egg 	2000-5000	To obtain immunized eggs, hens are repeatedly vaccinated against specific bacteria so their eggs will contain protective avian immunoglobulins (IgY). [13] Afterwards, the egg is spray dried into a powder. The product contains a mix of the full egg content.	Chickens are inexpensive and easier to handle than cows. Non-invasive production method for harvesting immunoglobulins. Contains egg allergen.
IgG Binding Protein			
Precision fermentation 	150-300	IgG Binding Proteins are derived from camelid immunoglobulins (IgGs) and produced through precision fermentation, making them animal-free. They have been designed and screened for their ability to bind harmful bacterial risk factors. Since IgG Binding Proteins are produced by microbial fermentation, there will be other fermentation products in this concentrate such as proteins, carbohydrate and dietary fiber present.	Precision fermentation offers a sustainable and consistent alternative to animal production. IgG Binding Proteins are derived from Camelid Immunoglobulins, which are considered more stable than traditional immunoglobulins. [14] Animal-free.

Table 1: Overview of common Immunoglobulin supplements and comparison to novel food ingredient IgG Binding Protein LT. *While there is no standardized dosage for BC, most clinical studies use between 10-60 g per day.[15]

The next step in gut health products - Enter IgG Binding Proteins

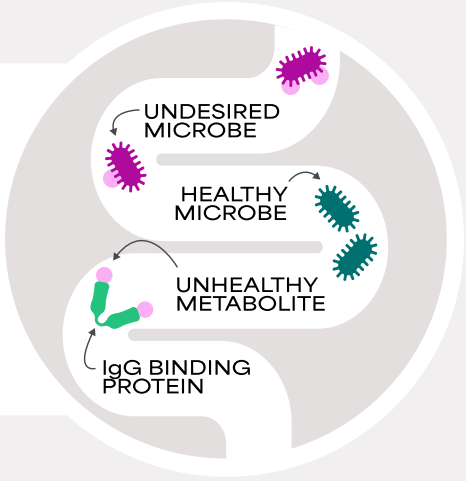
IgG Binding Proteins represent a novel class of functional protein ingredients for supporting gut health. The ingredients are derived from the binding domain of camelid immunoglobulins, making them an ideal alternative to conventional immunoglobulin products.[16] Furthermore, IgG Binding Proteins are produced via precision fermentation, ensuring consistent quality without the use of animals in production. Where conventional immunoglobulin supplements promote the microbiota's capacity to resist threats, IgG Binding Proteins act directly on unwanted metabolites, offering targeted, consistent, and customizable support. They are documented to bind unwanted metabolites, enabling their safe passage through the gastrointestinal tract,[17-19] thus avoiding downstream gut effects such as inflammation and degradation of the gut barrier, and helping to support gut stability in a gentle and effective manner. The ingredient offers a favorable safety profile for its intended uses in food and beverages, supported by both toxicity study and in silico allergenicity assessment, together which have demonstrated the safety of consuming IgG Binding Proteins. [20]

The IgG Binding Protein gut health effect

01 Fortifies the gut defense system
Binding Proteins neutralize disruptors

02 Avoid inflammatory response
Avoids inflammation by blocking uinhealthy metabolites before they can trigger immune responses

03 Supports a healthy gut barrier
Helps strengthen the intestinal barrier



Investigating the power IgG Binding Proteins

Undesired microbes can release unhealthy metabolites in the gut, which disrupts normal gut function and cause fluid loss, local inflammation, and weakening of the gut barrier. As an example, LT toxin from enterotoxigenic E. coli (ETEC), the most common cause of traveler's diarrhea, can trigger intestinal cells to release fluids and electrolytes.[21,22]

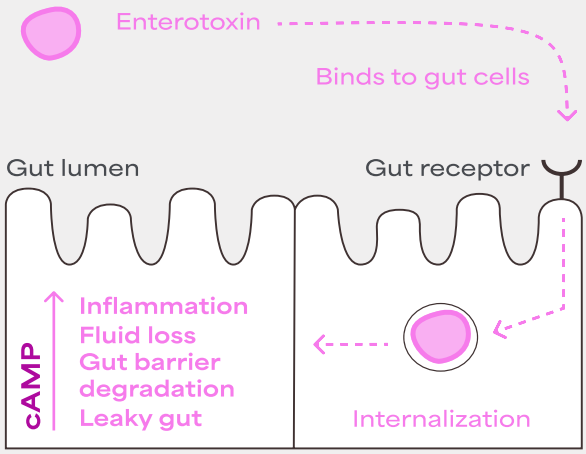
The fluid loss disrupts the gut barrier, especially tight junctions (the 'glue' between cells), causing increased gut permeability and release of inflammatory signals such as interleukin-8 (IL-8). Unlike lipopolysaccharide (LPS), a bacterial cell wall component found on Gram-negative bacteria and present both in the healthy microbiota and unwanted bacteria,[23] LT toxin is ETEC-specific. As a result, the toxin can be directly targeted and blocked without compromising a healthy, diverse microbiota.

In order to investigate the ability of different immunoglobulin supplements to strengthen the gut barrier against unhealthy metabolites such as LT toxin from ETEC, in vitro studies have been conducted, including two BC products (Referred to as BC1 and BC2), one SBI product, one IgY product and the novel food ingredient IgG Binding Protein LT. In these studies, three markers were used to examine cells in distress: cyclic adenosine monophosphate (cAMP), IL-8 and tight junctions.

cAMP

Plays a crucial role in regulating fluid and electrolyte movement in the intestine.

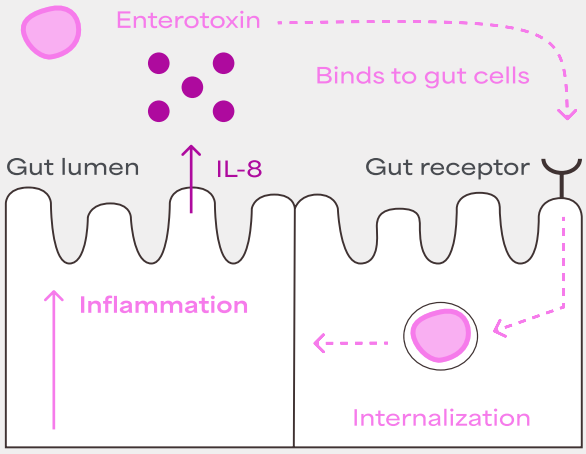
Elevated levels of cAMP in the cells leads to increased fluid secretion, which can disrupt digestion and nutrient absorption.



IL-8

IL-8 (Interleukin-8) is an inflammatory marker which the cells use to respond to pathogens and toxins.

Measuring IL-8 helps assess immune responses and the effectiveness of inflammation control.



Tight junctions

Tight junctions play an integral part of gut barrier integrity, since junctional proteins tightly bind intestinal cells together.

When these proteins are disrupted, the barrier becomes dysfunctional and leaky.

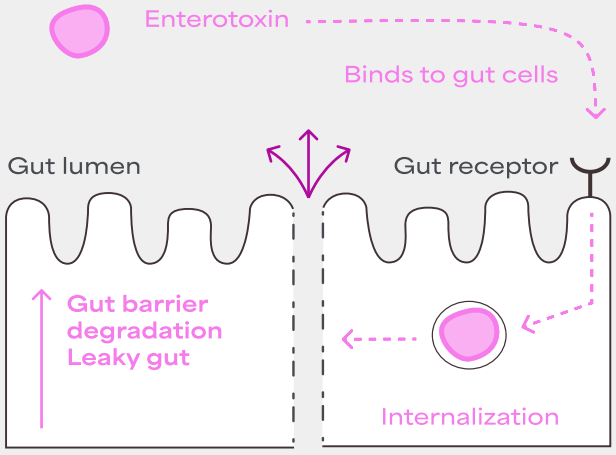


Figure 1: Simple visualization of three known markers indicating cells in distress.

Experimental setup

The most optimal concentration of each product was determined using a cell proliferation assay as according to Playford et al. 2020.[24] To simulate the intestinal cell layer two human colonic cell lines were utilized: HCA-7 for measuring cell conversion of ATP to cAMP, and T84 for investigating inflammation and cell barrier disruption. For the cAMP assay, combinations of toxin (0.2 µg/ml) with different immunoglobulin supplements were added to cells seeded 24 hours prior. After 2-hour incubation the cells were lysed and cAMP levels measured. For the IL-8 assay, cells were seeded 14-18 days prior to experiment, to obtain a confluent, differentiated monolayer representing the intestinal barrier. Combinations of toxin (0.1 µg/ml) with different immunoglobulin supplements were added to cells and incubated together for a day. Afterwards, IL-8 concentration was quantified in the cell supernatant using ELISA. To visually inspect the tight junction distribution after treatment, the cells were fixed and stained with Phalloidin.

IgG Binding Protein LT fortifies the gut defense system

IgG Binding Protein LT is documented to neutralize disrupters such as LT toxin from being absorbed by intestinal cells.[20] In an in vitro cell model, IgG Binding Protein LT could block LT toxin uptake, whereas the broad immunoglobulin supplements showed no inhibition.

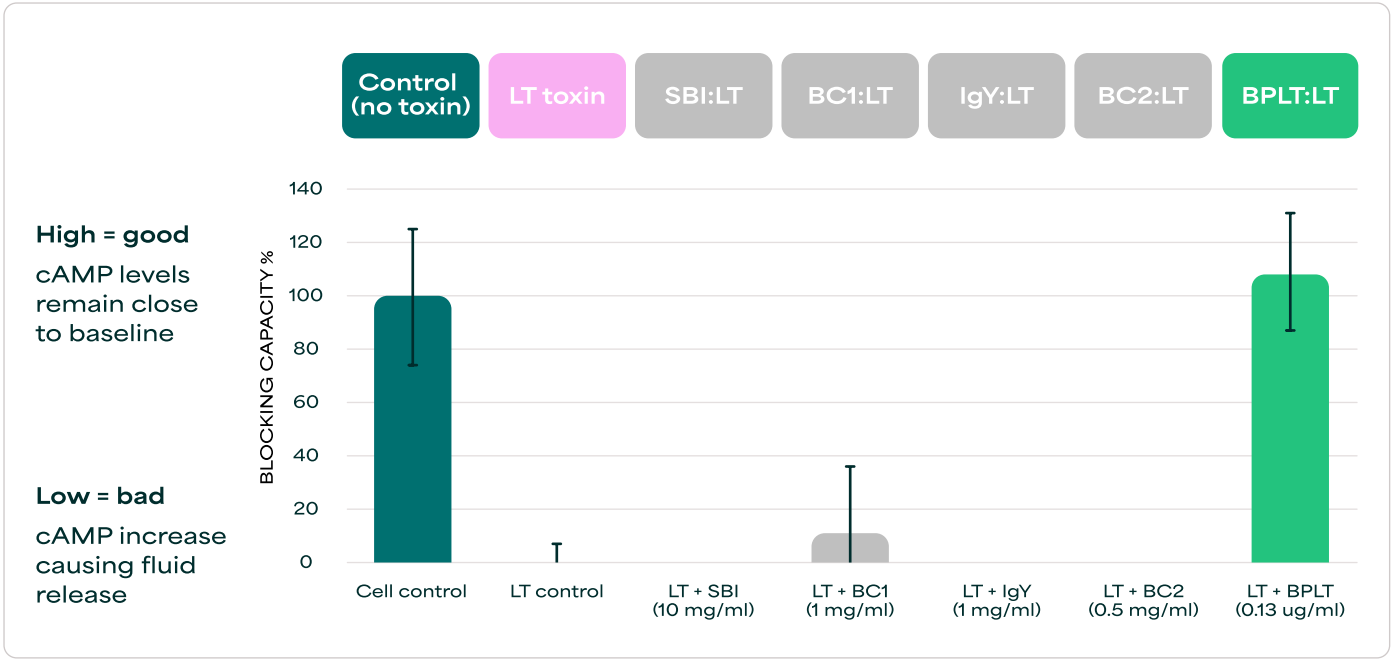


Figure 2: Intestinal cell assay measuring the blocking capacity of different supplements tested. By blocking disrupters such as LT toxin, the intestinal cells are kept intact, and the gut barrier is protected from disruption. BPLT = Binding Protein LT.

IgG Binding Protein LT avoid inflammatory responses

When the gut barrier integrity is compromised, tight junctions loosen and the epithelium becomes more permeable, triggering an immune response (e.g. release of immune signaling molecules called cytokines). This can drive local inflammation and further cause impairment on the gut barrier. In an in vitro intestinal cell model, IgG Binding Protein LT blocked LT toxin uptake, and no increase in inflammatory signals was observed when cells were exposed to both LT toxin and IgG Binding Protein LT together. The tested immunoglobulin supplements did not reduce inflammation in the presence of LT toxin.

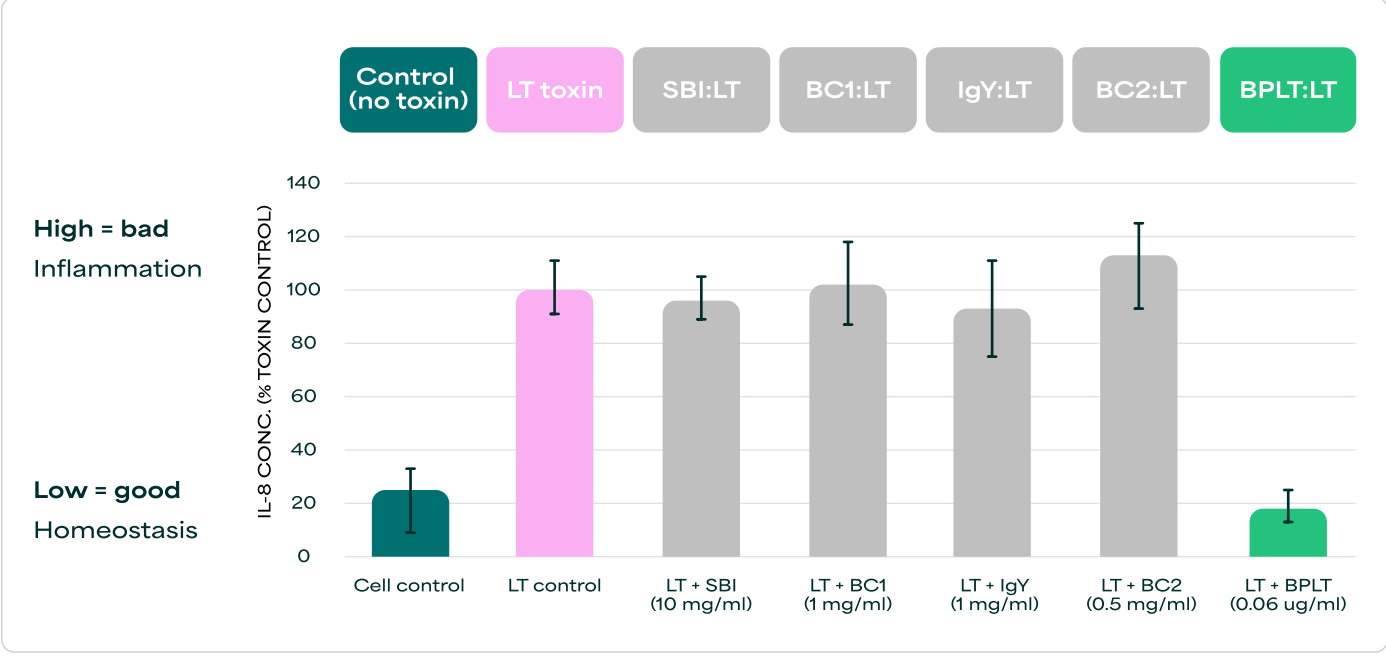


Figure 3: Intestinal cell assay measuring release of IL-8 (immune signaling molecule) from the cells after exposure to LT toxin in combination with different supplements. By blocking the LT toxin, IgG Binding Protein LT helps keep the intestinal cell barrier in balance, eliminating the need for immune activation. BPLT = Binding Protein LT.

IgG Binding Protein LT supports a healthy gut barrier

The gut barrier helps prevent unhealthy substances from entering the bloodstream while allowing essential nutrients to be absorbed. By blocking LT toxin, IgG Binding Protein LT contributes to the gut defense system by helping maintain the strength and integrity of the gut barrier.

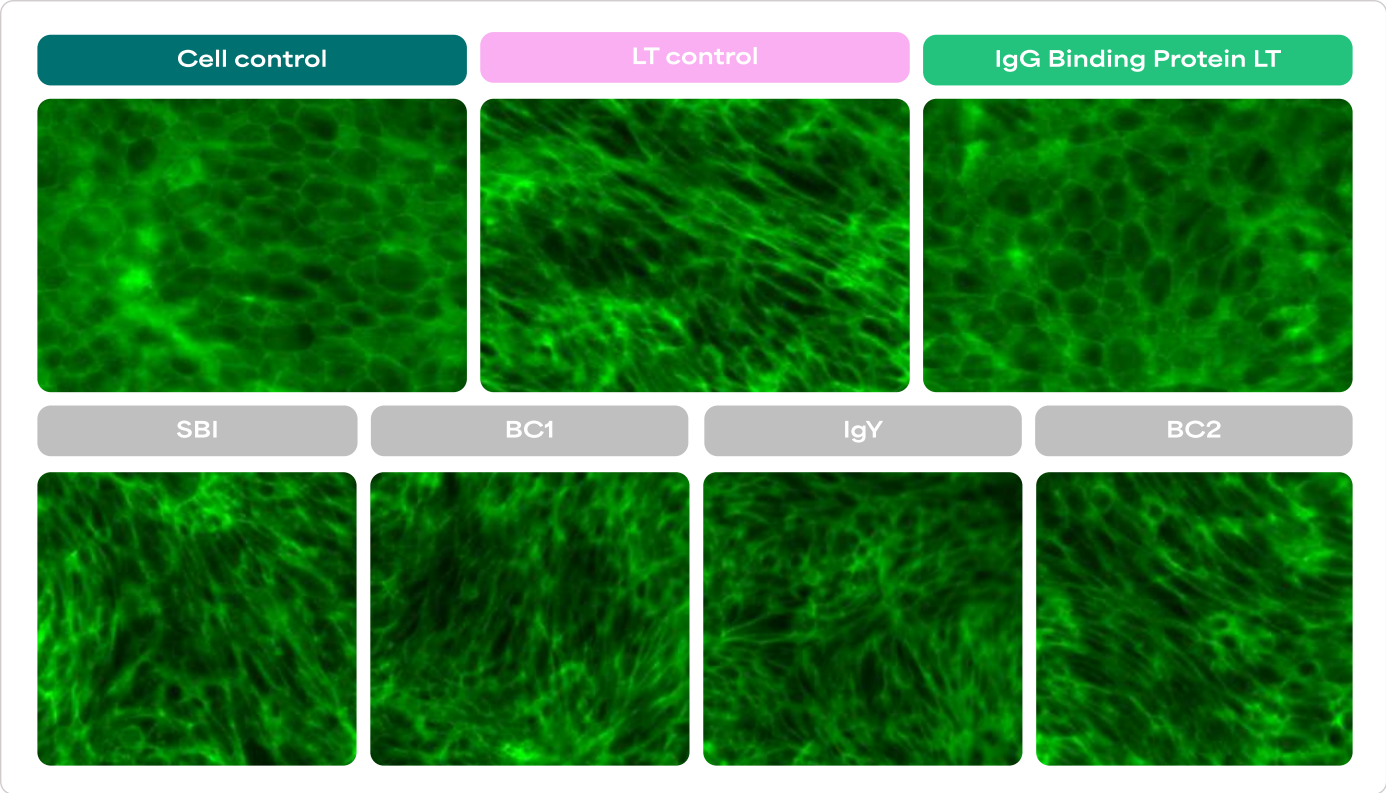


Figure 4: Fluorescence microscopy of confluent T84 cell layer stained with Phalloidin. The images show how the tight junction protein F-actin localizes in healthy (cell control) and disrupted (LT toxin) state. By blocking the LT toxin, IgG Binding Protein LT helps prevent the honeycomb structure of the intestinal cells from being disrupted.

Conclusion

IgG Binding Proteins present a novel food category offering targeted, low-dose, vegan options for supporting gut health in at-risk consumers. This includes travelers, people experiencing occasional GI discomfort, and immune challenged individuals. The novel ingredient is backed by strong safety data and can be integrated in various products such as dietary supplements, functional beverages and dairy products.

The study presented here illustrates how IgG Binding Protein LT protects the intestinal cell barrier from disruption and reduce immune activation by neutralizing the unhealthy metabolite LT toxin from ETEC. Even in low amounts IgG Binding Protein LT demonstrated superior ability to support gut barrier integrity while lowering inflammation in the presence of LT toxin.

In conclusion, IgG Binding Protein LT has the potential to benefit overall gut health, either alone or alongside existing gut support strategies, by helping maintain a strong intestinal barrier and protecting the cells from undesired metabolites in at-risk situations.

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