ImmunoLin® for Digestive Health and Immune Support

FAQ’s

ImmunoLin® is a protein-based (>90%) dietary supplement containing over 50% (w/w) immunoglobulins that helps support digestive function and a healthy mucosal immune system. The protein mixture found in ImmunoLin® is serum-derived bovine immunoglobulin/protein isolate (SBI) and is manufactured using a tightly-controlled and highly reproducible process at an FDA-inspected facility. Research studies provide evidence that the diversity of immunoglobulins and proteins found in ImmunoLin® are safe and help improve digestive health and nutritional status by decreasing immune activation through mechanisms that involve antigen binding and strengthening gut barrier function.
HEALTHY DIGESTIVE SYSTEMS, GI DISTRESS AND BUILDING IMMUNITY

A healthy digestive system breaks down foods and liquids into carbohydrates, fats, and proteins so the body can absorb them as nutrients for growth and energy. It also contains much of the body’s immune system, protecting against pathogens or other toxic substances consumed in food or water.

As with all complicated systems, the human digestive tract doesn’t always run smoothly. Problems caused by genetics, pathogenic microbes, or dysregulation of the immune system may cause gastrointestinal (GI) distress, resulting in symptoms such as bloating, abdominal pain, gas or diarrhea.

A way to support a healthy GI system is to consume active immune factors from another immunologically ‘mature’ individual, and is best documented through the ingestion of breast milk containing high levels of immunoglobulins by a newborn infant (1).

FREQUENTLY ASKED QUESTIONS REGARDING IMMUNOLIN®

Q WHAT IS IMMUNOLIN®?

A ImmunoLin® is the branded ingredient serum-derived bovine immunoglobulin/protein isolate (SBI). SBI is an agglomerated powder purified from edible bovine plasma using a tightly-controlled cGMP manufacturing process at an FDA-inspected facility.

Q WHAT IS THE COMPOSITION OF SBI?

A SBI is comprised of over 90% protein and consists of more than 50% immunoglobulins, other peptides and growth factors found naturally in milk or colostrum. Proteomics techniques have identified over 180 unique proteins in SBI. A complete product specification sheet for ImmunoLin®/SBI is available upon request.

Q HOW DOES SBI WORK?

A The mechanism by which immunoglobulins and other bioactive peptides found in SBI help to maintain gut barrier function is believed to involve the direct binding of microbial components found naturally in the digestive tract. In vitro studies have demonstrated that SBI binds to many potentially toxic microbial
antigens that appear normally in the intestinal tract (see list of microbial components proven to bind to SBI in Table 1).

These microbial antigens (e.g. bacterial endotoxin) are present in the intestinal tract due to the normal breakdown and turnover of resident bacteria and/or result from the consumption of contaminated food or water. These molecules (microbial antigens) have the potential to activate the intestinal immune system if they pass through a damaged intestinal epithelium. By binding to these microbial antigens (Table 1), SBI helps to create a complex so large that it has difficulty penetrating the intestinal epithelium, allowing instead for the antigenic complex to remain in the intestinal lumen and exit the intestinal tract following normal peristalsis.

To demonstrate this action, Detzel, et al. (2) conducted a study using an in vitro cell culture model to show that binding of antigens by the immunoglobulins in SBI prevented translocation of the antigens across epithelial cells, which in turn avoided the production of inflammatory cytokines by adjacent immune cells. These results suggest that the binding action of immunoglobulins in SBI helps keep toxic antigens within the lumen of the intestinal tract and avoid their absorption into the blood stream, which may help manage gut permeability and immune activation that occur with exposure to such antigens (2).

<table>
<thead>
<tr>
<th>Table 1. ImmunoLin binds a variety of bacterial antigens</th>
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<tr>
<td>SBI Binding Component</td>
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<tr>
<td>Lipopolysaccharide (LPS)</td>
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<tr>
<td>Flagellin</td>
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<tr>
<td>Lipoteichoic acid (LTA)</td>
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<tr>
<td>PAM3CSK4</td>
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<tr>
<td>Poly I:C</td>
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<tr>
<td>Cytosine-p-guanine dinucleotides (CpG)</td>
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<tr>
<td>C. difficile toxins A &amp; B</td>
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<tr>
<td>Helicobacter pylori</td>
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<td>Listeria monocytogenes</td>
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<td>Mycoplasma spp.</td>
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**WHAT ARE THE FUNCTIONAL HEALTH BENEFITS OF SBI?**

The following benefits of SBI have been observed in both animal and human studies:

SBI Supports Digestive/Gut Health. Immunoglobulin-containing serum protein preparations (like SBI) have been shown to consistently improve food intake and other nutritional parameters in a variety of animal species (3). Torrallardona (4) summarized the results from over 70 animal studies showing that immunoglobulin-containing plasma protein preparations (like SBI) led to improvements in caloric intake and metabolism of nutrients following supplementation in healthy animals. This research has led to the extensive use of plasma protein isolates as an animal feed component since the 1980’s to support and maintain health of weanling domesticated animals (5).

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SBI Supports Healthy Gut Barrier Function. Animal models have been utilized to assess the effect of SBI on supporting gut barrier function. In a rodent model of intestinal inflammation SBI supplementation prevented unwanted changes to specific markers of gut barrier function. In another study of intestinal inflammation mice supplemented with SBI maintained colon mucosal height, cecal stromal structure, and colonic glandular tissue, when compared to mice treated similarly but supplemented with a placebo protein.

SBI Helps Maintain Intestinal Homeostasis. Intestinal homeostasis refers to the overall “balance” of a functioning, healthy intestinal tract, and is critical for optimal nutrient utilization and immune function. SBI helps maintain intestinal homeostasis by supporting digestive function and maintaining a healthy mucosal immune system through mechanisms that involve antigen binding and strengthening gut barrier function. Human clinical studies have illustrated the nutritive effect of SBI supplementation on intestinal homeostasis.

SBI Maintains Immune Support. Animal models and human studies have evaluated the effect of SBI on intestinal immune function. Perez-Bosque and colleagues studied intestinal inflammation in mice and found SBI supplementation led to significant decreases in the expression of proinflammatory cytokines in gut mucosal tissue, while simultaneously increased levels of certain anti-inflammatory peptides. In another study involving mice, SBI resulted in significantly lower concentrations of serum markers for acute gut inflammation and epithelium damage. Plasma immunoglobulin concentrates (like SBI) have also been shown to support the health status of pigs that were experimentally infected with enterotoxigenic Escherichia coli K88.

In an open-label human clinical study, subjects given SBI had increased CD4+ counts in the duodenum. In a larger multicenter, placebo-controlled follow-up study, SBI led to significant increases in peripheral CD4+ cells, when compared to placebo-controlled subjects. The same study found significant decreases in circulating levels of interleukin-6 (a proinflammatory cytokine) and markers of intestinal barrier damage and enterocyte death in subjects who received SBI.

Q WHAT DATA IS AVAILABLE TO SUPPORT THE SAFETY OF SBI?
A Numerous animal and human studies have been conducted to provide evidence of the safety of SBI, including clinical trials involving over 234 subjects and published retrospective chart reviews describing the use of SBI by approximately 298 subjects. In total, over 530 subjects have been exposed to SBI in documented clinical studies for a minimum of 1 day to a maximum of 24 months with doses ranging from 5 g to 20 g per day. There are no known side effects associated with consumption of SBI.

Q WILL SBI NEGATIVELY IMPACT THE EFFICACY OF DAILY PROBIOTICS?
A No. While the immunoglobulins in SBI have been shown to bind to a variety of microbial antigens that are associated with immune activation, evidence from preclinical studies have shown the following: 1) SBI does not adversely affect the growth of probiotic or commensal bacteria in vitro and 2) SBI did not change the composition of the intestinal microbiota in an animal model used to evaluate host-microbiota relationships. No significant changes in commensal microflora have been observed following oral administration of SBI in humans, thus making SBI an excellent choice for consumers to use in conjunction with their daily probiotic supplementation.
HAS SBI RECEIVED A US FOOD AND DRUG ADMINISTRATION’S GRAS DESIGNATION

Yes. “GRAS” is an acronym for Generally Recognized As Safe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), a substance identified as GRAS is one that is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use. On December 24, 2008, the US FDA issued a letter assigning SBI (identified as “Bovine globulin”) GRAS notice No.255. The letter was issued in response to the application for GRAS designation reads, “Based on the information provided by Proliant [a sister company to Entera Health, Inc.], as well as other information available to FDA, the agency has no questions at this time regarding Proliant’s conclusion that bovine globulin is GRAS under the intended conditions of use.” (see reference 14).

DOES SBI CONTAIN COMMON, ALLERGENIC SUBSTANCES?

ImmunoLin® contains immunoglobulin protein isolate (SBI) and lecithin and does not contain milk products such as lactose, casein, or whey. SBI is a purified product that is gluten-free, dye-free, and soy-free and manufactured in accordance with current Good Manufacturing Practice (cGMP). However, since SBI is derived from a beef source, individuals who have an allergy to beef should not take this product.

WHAT IS THE RECOMMENDED SERVING SIZE / DOSE OF IMMUNOLIN® (SBI) AS A DIETARY SUPPLEMENT?

The recommended daily dose of ImmunoLin® is 1000-2000 mg per day. ImmunoLin® doses may be supplemented multiple times daily. This daily dose of ImmunoLin® is intended to supplement the body’s normal production of immunoglobulins in the healthy digestive tract, which has been reported to be from 3000 - 5000 mg/day.

KEY POINTS

- ImmunoLin® is the branded ingredient serum-derived bovine immunoglobulin/protein isolate (SBI).
- ImmunoLin® aids in the support of healthy gut barrier function and immune balance.
- ImmunoLin® is >90% protein and typically contains ~ 60% immunoglobulins (>50% IgG, ~5% IgM, ~1% IgA).
- ImmunoLin® binds to microbial antigens, including lipopolysaccharides (LPS), which helps to limit antigen absorption.
- There are no known side effects associated with consumption of ImmunoLin®.
- Safety and digestive health benefits of ImmunoLin® are documented in human clinical trials.
- Non-allergenic protein sourced from all natural and high-quality materials.

www.enterahealth.com/immunolin

ImmunoLin®
REFERENCES


For more information please submit an inquiry on our website located at: www.enterahealth.com/immunolin