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# **Key Features:**

- Dairy-Free, Gluten-Free, Soy-Free
- Multi-Strains (10-13)
- Bile & acid resistance test (no enteric coating required)
- Human-gut anchoring ability test
- · Antibiotic resistance panel to ensure safety
- 36-month Stability Test



### Supreme-PB30+ DF

For IBS, candidiasis, celiac disease, food sensitivity/ leaky gut syndrome, dyspepsia, peptic ulcer disease, as well as prevention of acute infectious and antibiotic-associated diarrhea.

.....



# Ultra-PB100+ DF

Powdered, high-dose probiotic formula for easy dose adjustment. Also suitable when higher dose is desired, such as in inflammatory bowel diseases (IBD).



#### Optimum-PB10+ DF

For prevention of dysbiosis caused by antibiotics and general immune and digestive support.

#### Baby & Mom-PB15+ DF



infants, toddlers, and pregnant/ breastfeeding moms. Contains effective strains to promote healthy development and prevent atopic disease for babies, and reduce the risk of gestational diabetes.



# S. boulardii

diarrhea, acute traveller's diarrhea, C. difficile infections, and decrease side effects during H. pylori eradication treatment.

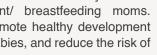
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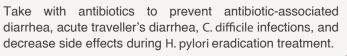
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- ATCC®-Registered monitoring strain identity, safety, and quality
- Contain up to 200% viable cells when manufactured
- · Suitable for all age groups and tailored to meet specific needs
- Comes with or without Fructooligosaccharides (FOS) prebiotic (except for Baby & Mom-PB15+)

















# **Clinical Evidence of Featured Strains**

### Bifidobacterium bifidum Bb-06<sup>[1]</sup>

*B. bifidum* has been shown to help reduce the risk of cold & flu as well as increase recovery time.

A study with 581 academically stressed undergraduate students received 3 billion cfu/day of probiotic L. helveticus, B. infantis, B. bifidum or placebo for 6 weeks. The results showed that B. bifidum supplementation resulted in a higher proportion of healthy days and a lower percentage of students reporting a day of cold/flu.

## Bifidobacterium lactis BL-04<sup>[2]</sup>

*B. lactis* BI-04 is effective in supporting the immune system and reducing the risk of respiratory infection in a clinical trial.

A total of 465 participants (241 males; 224 females) were randomly divided into 3 groups. One group had 2 billion cfu of *B. lactis* BL-04 only; the second group had 5 billion cfu of *L. acidophilus* NCFM + *B. lactis* BI-07, and both groups were compared to the placebo group. A 5-month intervention showed that only the *B. lactis* BL-04 group had a significantly lower risk of URTI by 27% (risk ratio of 0.73; p=0.02) compared to placebo. BL-04 also delayed the first onset of URTI by ~0.8 months.

# **Antibiotic Resistance Test** & Genome Database

Bacteria, including probiotics, are capable of sharing their genetic materials (e.g., plasmids); such nature could be problematic as the antibiotic-resistant genes from probiotics can potentially be passed onto the pathogenic bacteria. Antibiotic resistance test ensures that the probiotic strains are sensitive to at least 3 commonly used antibiotics, especially the last-resort ones such as Vancomycin, and Carbapenems. Moreover, all probiotics should have their genomes assayed and registered with public genome databases so that their safety and efficacy can continue to be monitored.

### Lactobacillus rhamnosus (Lr-32, HN001, GG)

L. rhamnosus is part of normal human gut flora. Among many other benefits, L. rhamnosus is known to balance the immune system, as clinical trials have shown efficacy on the prevention/recovery of infectious disease, allergies, and atopic dermatitis.

#### Lactobacillus rhamnosus HN001

L. rhamnosus HN001 has been clinically shown to reduce the risk of allergies (skin and respiratory systems) in children, as well as gestational diabetes in pregnancy.

### Eczema and Allergic sensitization: A 6-year RCT<sup>[3]</sup>

A double-blind, randomized, placebo-controlled trial of 316 mothers and their infants (placebo, n=159; HN001, n=157). Pregnant mothers were supplemented daily from 5 weeks preterm to 6 months post-term if breastfeeding. Infants were supplemented daily from birth until 2 years old.

At 2 years of age, the prevalence of eczema decreased by 49% (p=0.01) with supplementation. This effect persisted until 6 years of age with 44% lower prevalence (p=0.01).

In addition, HN001 showed a 31% decreased prevalence of positive skin-prick tests (p=0.04), and 62% less relative risk of rhinoconjunctivitis (rhinitis and red eyes).

#### Gestational diabetes mellitus (GDM) risk reduction<sup>[4]</sup>

In an RCT, pregnant women were randomized at 14-16 weeks of gestation to receive 6 billion of HN001 (n=212) or placebo (n=211) daily. At 24-30 weeks, GDM prevalence was significantly lower in the HN001 group, 2.1 % (CI=0.6-5.2), vs. 6.5 % (CI=3.5-10.9) in the placebo group (P=0.03). A significant association of lower GDM was reported in women aged ≥35 years (RR=0.31; CI=0.12-0.81, P=0.009) and those with a history of GDM (RR=0.00; CI=0.00-0.66, P=0.004).

#### Lactobacillus rhamnosus GG

L. rhamnosus GG is by far the most studied probiotic strain. Studies have shown its effectiveness from general to severe GI/ respiratory/ dental infections, as well as reducing allergy and IBS in infants and children.

#### Gastrointestinal Health<sup>[5], [6], [7]</sup>

L. rhamnosus GG is known to be one of the most effective probiotics in reducing both severity and duration of acute onset infectious diarrhea (overall reduction 1.05 days). Several systemic reviews and meta-analysis studies also suggest a protective effect of L. *rhamnosus* GG against antibiotic-associated diarrhea, preterm neonatal Candida, Clostridium difficile induced colitis, vancomycinresistant enterococci, and improvement of abdominal pain in children with IBS (NNT=4).

### Respiratory and Atopic Diseases Prevention

In additional to GI conditions, L. rhamnosus GG was effective in reducing the risk of respiratory tract infection in preterm infants and hospitalized children, as well as in protecting hospitalized patients and patients with cystic fibrosis against *Pseudomonas aeruginosa* pneumonia.

Another area for *L. rhamnosus* GG application is in the pre- & postnatal period. Prenatal supplementation of *L. rhamnosus* GG was shown to promote a beneficial profile dominated by bifidobacteria in neonates. An RCT involving 105 infants fed standard infant formula supplemented with L. rhamnosus GG developed better than the control group.<sup>[8]</sup> Two meta-analyses provided the best evidence for L. rhamnosus GG supplementation in mothers and infants in the long-term prevention of atopic dermatitis.<sup>[9]</sup>

#### Oral Health

Milk containing *L. rhamnosus* GG has been demonstrated to reduce dental caries and lower Streptococcus mutans levels in dental plaque and saliva. [10]

### Lactobacillus reuteri 1E1

L. reuteri helps reduce the time of crying in infantile colic and promote recovery in acute infectious diarrhea.

# "Human Strains" v.s. "Human Gut Anchoring Strains"

Humans are born sterile before they encounter a variety of bacteria from their surroundings. Therefore, even though "human strain" is one of the highly marketed features in probiotic formulas, there is no strain from human origin. Any strains of bacteria succeeded in colonizing in their host human become the "human strains". Probiotics' human-gut anchoring ability can actually be tested via their adhesion to human intestinal cell lines – HT-29 and Caco-2.

One meta-analysis of 3 RCTs on infantile colic (n=209) showed L. *reuteri* supplementation reduced risk of infant crying time at 14 and 21 days (NNT = 2). [11]

S. boulardii is the most studied yeast probiotic. Research has documented efficacy of S. boulardii for the treatment of acute gastroenteritis, especially in children, and for the prevention of The other meta-analysis of 8 RCTs involving 1,229 children found antibiotic-associated diarrhea, both in adults and children. There that L. reuteri supplementation reduced the duration (25 hours) of is also evidence supporting the use of S. boulardii to increase the acute infectious diarrhea and increased the cure rate on days 1 and eradication rate of Helicobacter pylori and decrease antibiotic side 2. [12] effects. [19]

### **Bifidobacterium infantis Bi-26**

Other clinical uses of S. boulardii include improved weight gain B. infantis is passed from mother to baby during vaginal birth and is and feeding tolerance in preterm infants <sup>[20]</sup>, reduced bacterial considered a superior colonizer of the infant gut due to its unique translocation and inflammatory markers in HIV patients<sup>[21]</sup>, as well ability to digest oligosaccharides in human milk.[13] as a lowered coronary artery disease biomarker in patients with Naturally, B. infantis helps with proper metabolic and immune hypercholesterolemia. [22]

development of the infants. However, with the growing practice of C-section, avoidance of breastfeeding, and exposure to antibiotics in mother's life, colonization of B. infantis has been mostly eliminated in babies born today, which leads to dysbiosis and detrimental consequences in the baby's life.

Preclinical data have shown that *B. infantis* has anti-inflammatory activity, and could decrease intestinal permeability in premature intestinal cells. In premature infants, *B. infantis* was found to decrease Enterobacteriaceae (e.g., Salmonella, E. coli, Klebsiella, and Shigella) and reduce the risk of necrotizing enterocolitis. Colonization with *B. infantis* is also associated with better weight gain, increased thymic index, and better response to vaccines.

In a phase I clinical trial, B. infantis supplement was safe and welltolerated and showed fewer and better-formed stool in healthy term breastfed infants, compared to "frequent, watery" stool in the control group.<sup>[14]</sup>

Multiple clinical trials and a meta-analysis found B. infantis supplementation significantly relieves many IBS symptoms (i.e., abdominal pain, gas/bloating, bowel dysfunction), as well as normalization of inflammation markers. The effect on bloating/ distension was more prominent with B. infantis in a composite formula.[15,16, 17,18]

Dairy Free Probiotic	Supreme-PB30+	**Ultra-PB100+	Optimum-PB10+	**Baby & Mom-PB15+	S. boulardii
Size	56 veg caps*	28 servings (1 tsp)*	56 veg caps*	56 servings (1/2 tsp)	84 veg caps
Viable cells at time of manufacture (CFU)	Up to 55 billion	Up to 200 billion	Up to 18 billion	Up to 25 billion	
Lactobacillus acidophilus La-14	6 billion	15 billion	2.1 billion	1.5 billion	
Lactobacillus rhamnosus Lr-32	2 billion	15 billion	1 billion	1.5 billion	
Lactobacillus casei Lc-11	5 billion	10 billion	0.6 billion	1 billion	
Lactobacillus salivarius Ls-33	1 billion	8 billion	0.6 billion	1 billion	
Bifidobacterium bifidum Bb-06	1 billion	2 billion	0.4 billion	0.5 billion	
Bifidobacterium lactis BI-04	5 billion	12 billion	1.6 billion	1.5 billion	
Streptococcus thermophilus St-21	2 billion	8 billion	0.5 billion	1 billion	
Bifidobacterium breve Bb-03	1.5 billion	5 billion	0.6 billion	1 billion	
Lactobacillus plantarum Lp-115	1.5 billion	15 billion	1.5 billion	1.5 billion	
Lactobacillus rhamnosus GG	3 billion	6 billion	1.2 billion	2 billion	
Lactobacillus rhamnosus HN001	2 billion	3 billion		2 billion	
Bifidobacterium infantis Bi-26		1 billion		1 billion	
Lactobacillus reuteri 1E1		1 billion		0.5 billion	
Saccharomyces boulardii					5 billion

#### Saccharomyces boulardii

### Yeast Probiotic vs. Yeast Infection

Some may have concern that taking yeast probiotic such as S. boulardii might lead to Candida infection in otherwise healthy individuals has not been substantiated by clinical evidence. In fact, preclinical data showed inhibitory effect of *S. boulardii* on the ability to form filaments and biofilms of C. albicans [25]; S. boulardii could also reduce pro-inflammatory cytokine IL-8 expressed by C. albicansinfected intestinal cells.<sup>[26]</sup>

In a clinical study of preterm infants with low birth weight, prophylactic S. boulardii is as effective as nystatin for the prevention of fungal colonization and invasive infection. Moreover, S. boulardii reduce incidence and number of sepsis attacks significantly more than nystatin and showed better feeding intolerance.<sup>[27]</sup>

### Why Single Strain S. boulardii?

Although combination probiotics with S. boulardii are available on the market, existing clinical trials have been utilizing single-strain preparation. Possible antagonism may exist between yeast & bacteria and decrease therapeutic efficacy.<sup>[23]</sup> In a RCT on children with acute rotavirus diarrhea, significantly shortened duration of fever & diarrhea was seen with single-strain S. boulardii, but not with combination of *S. boulardii* + other probiotics. <sup>[24]</sup>