

Flora Daily + Sb



Clinical Applications

- Helps Maintain a Healthy Intestinal Microecology*
- Supports Bowel Regularity*
- Supports Gastrointestinal-Based Immunity*

Flora Daily + Sb is ideal for individuals seeking a well-rounded supplement to support a healthy balance of intestinal flora, cellular health, and immune health. It features four probiotic strains, including the extensively studied HN019 strain of *Bifidobacterium lactis*, plus *Saccharomyces boulardii* (Sb), a non-pathogenic yeast, to further complement healthy gastrointestinal ecology. Gastro-resistant, vegetarian capsules provide an innovative solution for targeted delivery of sensitive ingredients to the small intestine, as they alleviate exposure to the low pH environment of the stomach. Additionally, each capsule is sealed in a nitrogen-purged blister pack to provide protection from heat, moisture, and oxygen, factors known to compromise probiotic stability.*

All The 3rd Opinion Inc. Formulas Meet or Exceed cGMP Quality Standards

Discussion

Diversity of gut microflora is characteristic of a healthy GI microbiome and contributes to overall health and vitality by promoting optimum digestion, assimilation, gut integrity, motility, and efficient removal of toxins and wastes. Many internal and external influences, including stress, a poor diet, food sensitivities, medication, environmental factors, and certain disease conditions, can impact the microbial balance within this fine-tuned community. Their impact can allow potential colonization by pathogenic organisms and disrupt a healthy balance, which can result in adverse effects ranging from GI symptoms to impaired immune response.^[1-3] Probiotics are part of the key to promoting the optimal balance of the microbiome,^[4] whether they originate from dietary sources or from supplements. Probiotic yeasts, such as *Saccharomyces boulardii*, also play a role in gut ecology by supporting intestinal barrier function and integrity.*

Common challenges associated with probiotic supplementation are maintaining the stability of the organisms during distribution and shelf life and, after they are swallowed, the survival of the organisms as they travel through the digestive tract to the targeted tissue. To help ensure stability, The 3rd Opinion Inc. packages Flora Daily + Sb capsules in sealed, nitrogen-purged blister packs to serve as protection from factors proven to compromise the stability of probiotics, such as heat, moisture, and oxygen. Careful selection of organisms is another way The 3rd Opinion Inc. helps ensure stability and digestive survivability. To further support resistance to low pH and the delivery of microorganisms to the small intestines, The 3rd Opinion Inc. encapsulates the ingredients in gastro-resistant DRcaps™. These specially designed, innovative capsules help slow exposure of actives to stomach acid to promote a more targeted release.*

HOWARU® (*Bifidobacterium lactis* HN019) Discovered in 1899, *B. lactis* play a key role in the human microflora throughout a person's life. Researchers have identified strain HN019 as having excellent probiotic potential based on its ability to survive the transit through the human gastrointestinal tract, adhere to epithelial cells, and proliferate.^[5] *B. lactis* HN019 has been extensively studied, and its safety and effectiveness are well-accepted.^[6,7] To assess the impact of *B. lactis* HN019 supplementation on whole-gut transit time in adults, subjects (N = 100) were given daily doses of 17.2 billion colony-forming units (CFU), 1.8 billion CFU, or placebo for 14 days. Decreases in mean whole-gut transit time over the 14-day study period were statistically significant in the high-dose group and the low-dose group, but not in the placebo group.^[7] This level of dosing also supported other parameters of healthy GI function, as were self-reported by patient survey.^[7] In a randomized, double-blind, placebo-controlled human dietary intervention study, 80 subjects older than 60 years who took supplementary *B. lactis* HN019 had statistically significant increases in the beneficial organisms bifidobacteria and lactobacilli.*^[8]

***Lactobacillus acidophilus* (*Lactobacillus acidophilus* La-14)** This common inhabitant of the human microbiome is also found in some traditional fermented milks (e.g., kefir) and is widely used in probiotic foods and supplements with a history of safe human consumption. The *L. acidophilus* La-14 strain is of human origin and has been identified as a type A1 *L. acidophilus*, showing excellent adhesion to human epithelial cell-lines.*^[9,10]

***Lactobacillus plantarum* (*Lactobacillus plantarum* Lp-115)** Isolated from plant material, the *L. plantarum* strain is abundantly present in lactic acid-fermented foods, such as olives and sauerkraut. In vitro studies have shown that *L. plantarum* Lp-115 has excellent adhesion to epithelial cell lines.^[11] In addition, *L. plantarum* is resistant to low pH conditions and survives the presence of bile at duodenal concentrations.*^[11,12]

***Bifidobacterium longum* (*Bifidobacterium longum* BI-05)** The *B. longum* BI-05 strain is well-accepted as safe for human consumption. *B. longum* is resistant to low pH and bile salts and is well-suited to the intestinal environment.*^[12]

Saccharomyces boulardii *S. boulardii* might be most well-known by consumers for its role as the type of yeast used in the widely popular kombucha beverages. Extensive research in both European and American peer-reviewed journals has shown that this natural, non-pathogenic yeast has multiple mechanisms of action that support healthy gut ecology. In a 2010 systematic review and meta-analysis of 31 randomized placebo-controlled treatment arms in 27 trials (encompassing 5,029 adult study patients), *S. boulardii* was found to be significantly efficacious in 84% of those treatment arms.^[13] *S. boulardii* was also found to be efficacious for use in children in a double-blind, randomized, placebo-controlled

Continued on next page

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Distributed by:
The 3rd Opinion Inc.
P.O. Box 10

Chatanooga, OK 73528
1-800-431-7902

Flora Daily + Sb



Supplement Facts

Serving Size: 1 Capsule
Servings Per Container: 30

	Amount Per Serving	%Daily Value
<i>Saccharomyces boulardii</i>	250 mg (5 Billion CFU [†])	**
Proprietary Blend	174 mg (15 Billion CFU [†])	**
<i>Lactobacillus acidophilus</i> La-14 [®]		
<i>Bifidobacterium longum</i> BI-05 [™]		
<i>Lactobacillus plantarum</i> Lp-115 [®]		
HOWARU [®] Bifido	50 mg (15 Billion CFU [†])	**
<i>(Bifidobacterium lactis</i> HN019 [®])		
** Daily Value not established.		

Other Ingredients: Capsule (hypromellose, gellan gum, and water), microcrystalline cellulose, hydroxypropyl cellulose, ascorbyl palmitate, and silica.

† Colony-Forming Unit

HOWARU[®]

HOWARU[®] and the HOWARU[®] logo are registered trademarks of DuPont or its affiliates.

HN019[®] is a registered trademark of Fonterra[™] Limited and is licensed to DuPont Nutrition Biosciences.

Directions

Take one capsule daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Individuals taking medication should discuss potential interactions with their healthcare practitioner.

Does Not Contain

Wheat, gluten, soy, animal or dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or artificial preservatives.

References

1. Heiman ML, Greenway FL. A healthy gastrointestinal microbiome is dependent on dietary diversity. *Mol Metab*. 2016 Mar 5;5(5):317-20. [PMID: 27110483]
2. Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. *Genome Med*. 2016 Apr 27;8(1):51. [PMID: 27122046]
3. Xu Z, Knight R. Dietary effects on human gut microbiome diversity. *Br J Nutr*. 2015 Jan;113 Suppl:S1-5. [PMID: 25498959]
4. Grimm V, Riedel CU. Manipulation of the microbiota using probiotics. *Adv Exp Med Biol*. 2016;902:109-17. [PMID: 27161354]
5. Gopal P, Prasad J, Gill HS. Effects of the consumption of *Bifidobacterium lactis* HN019 (DR10TM) and galacto-oligosaccharides on the microflora of the gastrointestinal tract in human subjects. *Nutr Res*. 2003;23:1313-28. <https://www.optibacprobiotics.co.uk/uploads/gopal-2003-effect-of-HN019-and-GOS-on-microflora-in-GIT-in-humans.pdf>. Accessed January 9, 2018.
6. Danisco. Clinical study bibliography & abstracts. HOWARU[®] Bifido. <http://www.danisco.com/product-range/probiotics/howarur-premium-probiotics/howarur-bifido-probiotics/howarur-bifido-clinical-studies/#c21397>. Accessed January 9, 2018.
7. Waller PA, Gopal PK, Leyer GJ, et al. Dose-response effect of *Bifidobacterium lactis* HN019 on whole gut transit time and functional gastrointestinal symptoms in adults. *Scand J Gastroenterol*. 2011 Sep;46(9):1057-64. [PMID: 21663486]
8. Ahmed M, Prasad J, Gill H, et al. Impact of consumption of different levels of *Bifidobacterium lactis* HN019 on the intestinal microflora of elderly human subjects. *J Nutr Health Aging*. 2007 Jan-Feb;11(1):26-31. [PMID: 17315077]
9. Greene JD, Klaenhammer TR. Factors involved in adherence of lactobacilli to human Caco-2 cells. *Appl Environ Microbiol*. 1994 Dec;60(12):4487-94. [PMID: 7811085]
10. Kleeman EG, Klaenhammer TR. Adherence of *Lactobacillus* species to human fetal intestinal cells. *J Dairy Sci*. 1982 Nov;65(11):2063-69. [PMID: 7153393]
11. Collado MC, Meriluoto J, Salminen S. Role of commercial probiotic strains against human pathogen adhesion to intestinal mucus. *Lett Appl Microbiol*. 2007 Oct;45(4):454-60. [PMID: 17897389]
12. Ding WK, Shah NP. Acid, bile, and heat tolerance of free and microencapsulated probiotic bacteria. *J Food Sci*. 2007 Nov;72(9):M446-50. [PMID: 18034741]
13. McFarland LV. Systematic review and meta-analysis of *Saccharomyces boulardii* in adult patients. *World J Gastroenterol*. 2010 May 14;16(18):2202-22. [PMID: 20458757]
14. Riaz M, Alam S, Malik A, et al. Efficacy and safety of *Saccharomyces boulardii* in acute childhood diarrhea: a double blind randomised controlled trial. *Indian J Pediatr*. 2012 Apr;79(4):478-82. [PMID: 21997865]
15. Vandenplas Y, Brunser O, Szajewska H. *Saccharomyces boulardii* in childhood. *Eur J Pediatr*. 2009 Mar;168(3):253-65. [PMID: 19096876]
16. Can M, Besirbellioglu BA, Avci IY, et al. Prophylactic *Saccharomyces boulardii* in the prevention of antibiotic-associated diarrhea: a prospective study. *Med Sci Monit*. 2006 Apr;12(4):PI19-22. [PMID: 16572062]
17. Castagliuolo I, Riegler MF, Valenick L, et al. *Saccharomyces boulardii* protease inhibits the effects of *Clostridium difficile* toxins A and B in human colonic mucosa. *Infect Immun*. 1999 Jan;67(1):302-7. [PMID: 9864230]
18. Im E, Pothoulakis C. Recent advances in *Saccharomyces boulardii* research [in French]. *Gastroenterol Clin Biol*. 2010 Sep;34 Suppl 1:S62-70. Review. [PMID: 20889007]
19. Krasowska A, Murzyn A, Dyjankiewicz A, et al. The antagonistic effect of *Saccharomyces boulardii* on *Candida albicans* filamentation, adhesion and biofilm formation. *FEMS Yeast Res*. 2009 Dec;9(8):1312-21. [PMID: 19732158]
20. Natural Standard Database. *Saccharomyces Boulardii* Monograph. <http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=s&s=ND&pt=100&id=332&ds=>. Accessed January 9, 2018.
21. Buts JP, Bernasconi P, Vaerman JP, et al. Stimulation of secretory IgA and secretory component of immunoglobulins in small intestine of rats treated with *Saccharomyces boulardii*. *Dig Dis Sci*. 1990 Feb;35(2):251-6. [PMID: 2302983]
22. Dahan S, Dalmasso G, Imbert V, et al. *Saccharomyces boulardii* interferes with enterohemorrhagic *Escherichia coli*-induced signaling pathways in T84 cells. *Infect Immun*. 2003 Feb;71(2):766-73. [PMID: 12540556]
23. Pothoulakis C. Review article: anti-inflammatory mechanisms of action of *Saccharomyces boulardii*. *Aliment Pharmacol Ther*. 2009 Oct 15;30(8):826-33. Review. [PMID: 19706150]
24. Schneider SM, Girard-Pipau F, Filippi J, et al. Effects of *Saccharomyces boulardii* on fecal short-chain fatty acids and microflora in patients on long-term total enteral nutrition. *World J Gastroenterol*. 2005 Oct 21;11(39):6165-9. [PMID: 16273644]
25. Lewis K, Lutgendorff F, Phan V, et al. Enhanced translocation of bacteria across metabolically stressed epithelia is reduced by butyrate. *Inflamm Bowel Dis*. 2010 Jul;16(7):1138-48. [PMID: 20024905]

study that yielded statistically significant positive results for supporting normal gastrointestinal function in children aged 3-59 months.^[14] When safety data was examined in adult subjects (n = 2,963) in a trial of patients with *Clostridium difficile* infections, the adverse reactions associated with *S. boulardii* were minimal (<0.3%): thirst in five subjects and constipation in eight subjects.^[13] Another study in children aged three months and older demonstrated that *S. boulardii* can be used safely and effectively in this population group.^{*[15]}

With regard to maintaining normal GI function and transit time, research suggests that *S. boulardii* secretes a protease that may assist in directly degrading bacterial toxins and stimulating antibody production against those toxins.^[16-18] *S. boulardii* is also believed to exert a trophic effect on intestinal mucosa and positively support the immune system.^{*[14]}

This probiotic yeast appears to support normal gastrointestinal flora and integrity^[19,20]; promote production of intestinal enzymes and secretory IgA^[21]; and support cytokine balance through its effects on IL-8, IL-6, IL-10, NF-kappaB, TNF-alpha, and PPAR-gamma.^[18,22,23] Research also suggests a role for *S. boulardii* in the production of health-promoting short-chain fatty acids including butyrate, which supports homeostasis of colonic flora and fuels intestinal epithelial cells among its other benefits.^[24,25] The *S. boulardii* used in this formula is processed by low-temperature vacuum drying for improved stability.*

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

