



HOWARU® RESTORE

Promotes Good Digestive Health During Episodes of Gut Stress

Clinically-proven formulation for restoring gut health

Of all the organs in the human body, those of the gut are some of the most susceptible to external stress factors. Antibiotic treatment, travel, a poor diet, and a hectic way of life are just some of the stressors your GI tract may encounter on a daily basis. This can throw your beneficial bacteria off balance and undermine your body's natural defenses.

HOWARU® Restore combines top-quality lactobacilli and bifidobacteria strains in a clinically-proven formulation to address gut stress episodes and strengthen gut health.⁵

HOWARU® Restore is designed to provide equal upper and lower intestine support. The formulation is comprised of 50% by count of those bacteria that are adapted to the upper intestine—specifically the *Lactobacillus* species: *Lactobacillus acidophilus* (HOWARU NCFM™) and *Lacticaseibacillus paracasei* (HOWARU Lpc-37™) and 50% by count of the *Bifidobacterium* species, which are adapted to the lower intestinal tract. These strains are *Bifidobacterium lactis* (HOWARU Bi-07™) and *Bifidobacterium lactis* (HOWARU BI-04™).⁶

Product Attributes

17B CFU

Lactobacillus acidophilus
(HOWARU NCFM™)

Lacticaseibacillus paracasei
(HOWARU Lpc-37™)

Bifidobacterium lactis
(HOWARU Bi-07™)

Bifidobacterium lactis
(HOWARU BI-04™)

- ⊙ Addresses diarrhea & bloating
- ⊙ Fortifies with beneficial bacteria during times of dysbiosis/GI stress
- ⊙ Quickly restores gut health*

*duration of diarrhea was significantly reduced from average of 5.4 days to 2.6 days in a clinical intervention of probiotics compared to placebo



Gut Health Restored

Antibiotic-associated diarrhea (AAD) is experienced by 1 in 5 antibiotic users, which amounts to over 180 million people annually. Studies have shown that one of the most effective and natural ways consumers can overcome the negative effects of gut stresses, such as antibiotic therapy, is to supplement their diet with an efficacious dose of live and active probiotic bacteria.

The beneficial effect of probiotics when dealing with gut stressors such as antibiotic therapy was the subject of a large (N=503) clinical trial. This randomized, triple-blinded, placebo-controlled, dose-ranging study was conducted on healthy adults who were inpatient volunteers requiring antibiotic therapy.²

The study focused on the blend of the four probiotic strains contained in HOWARU® Restore with the primary aim of measuring the incidence of AAD and Clostridioides difficile (formerly Clostridium difficile) associated diarrhea (CDAD) during and after antibiotic use has been confirmed. The secondary objectives were to investigate the dose effect on the severity and duration of AAD and CDAD, the number of liquid stools per day, fever, bloody stools, bloating and abdominal pain. Subjects were stratified according to age (30–49 and 50–70 years), sex, and antibiotic treatment duration (3–8 and 9–14 days). HOWARU® Restore was administered from the start of antibiotic therapy and continued for 7 days after the cessation of antibiotic treatment. Those in the treatment group were further divided into high dose (10 x 10⁹ CFU/Day) and low dose (2.5 x 10⁹ CFU/Day)* groups.

Subjects taking the high dose of HOWARU® Restore experienced a 50% reduction in incidence of AAD compared to the placebo group (p<0.005) - see Figure 1. The subjects taking the low dose version showed a 20% reduction compared to that of the placebo group, but the results were not statistically significant.*

Subjects taking both the high and low dose of HOWARU® Restore experienced significantly reduced durations of diarrhea compared to the placebo with a 35% reduction for the low dose group and a 52% reduction for those taking the high dose formulation - see Figure 2. Both groups also experienced a significant (p< 0.05) reduction in the number of liquid stools per day with a 9% reduction for the low dose group and a 23% reduction for the high dose group. This probiotic blend has also shown some beneficial effects in regards to the reduction of undesirable GI symptoms during antibiotherapy as well as the reduction of incidences of C. difficile associated diarrhea (p=0.02) in the high dose group.

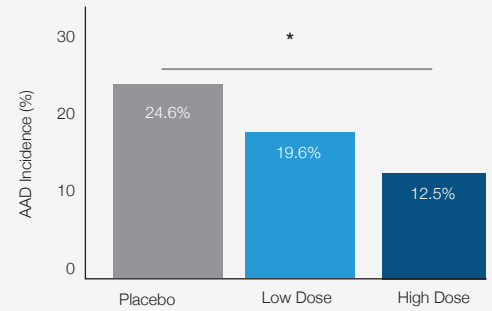
Clostridioides Difficile Associated Diarrhea (CDAD)

In a double-blind, placebo controlled, phase two clinical trial, patients who were diagnosed with a first episode of Clostridioides difficile (CDI) infection were assigned to either take HOWARU® Restore (17 x 10⁹ CFU/Day) or a placebo.³ The aim of the study was to evaluate the efficacy of probiotic treatment for reducing the duration of diarrhea and CDAD recurrence in patients with a first episode of CDAD (PICO study). The trial analyzed fecal samples to identify compositional changes in the GI microbiota that would be associated with the supplemental probiotic treatment.

The results showed that the median duration of diarrhea was one day shorter in the probiotic group than in the placebo group (p=0.039) and the total diarrhea days and rate of diarrhea were significantly better for the participants treated with probiotics than that of the placebo group.⁴ The results also found a significant treatment effect on the probiotic diversity (as measured by the Shannon diversity index) (p = 0.034) as seen in Figure 3.

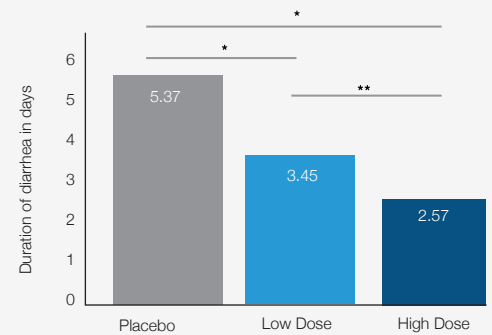
References

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- Ouwehand *et al.*; Vaccine: 2013
- Barker *et al.* Contemporary Clinical Trials 2015
- De Wolfe *et al.* Plos One 2018
- Rasinkangas & Ouwehand 2017 AgroFood Industry Hi-Tech 28 (4-5):18-22
- Forssten & Ouwehand, Microbial Ecology in Health & Disease 2017
- Barker *et al.* 2017 J Antimicrob Chemother



*P=0.05

Figure 1: Significant reduction of incidence of AAD



*p<0.001 **p=0.03

Figure 2: Significant reduction of the duration of diarrhea

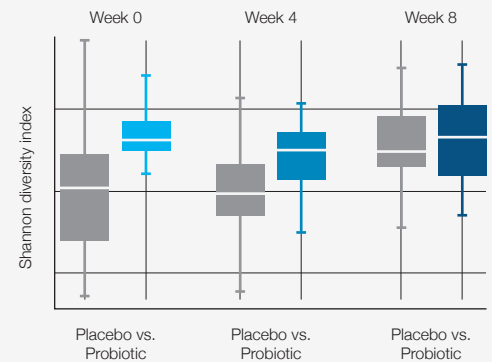


Figure 3: Significant effect on probiotic diversity. De Wolfe *et al.* 2018 PLoS ONE 13(9):e0204253.

*Actual inclusion (including overage): High Dose: 17 x 10⁹ CFU/Day, Low Dose: 4.17 x 10⁹ CFU/Day



OUR HOWARU® PROMISE

As a trusted global leader in probiotic solutions, we offer the broadest range of robust, clinically-studied strains. You can be confident that our extensive portfolio, strong consumer insights, and unmatched global support and services make us your ideal partner in probiotic innovation.







Our Strains Area:

- ✓ Backed by Science
- ✓ Identified with complete genome. Every strain has been sequenced and fully assembled
- ✓ Tested for virulence and toxigenic properties and the absence of antibiotic resistance transfer potential
- ✓ Tested for toxicity to confirm safety for human consumption
- ✓ Formulated and evaluated to ensure viability through end of shelf life
- ✓ Generally Recognized as Safe (GRAS) or FDA notified without objection as a New Dietary Ingredient
- ✓ Manufactured in the USA under FDA Good Manufacturing Practices

Exceptional Quality

-  High Performance
-  High Stability
-  High Functionality

Our Areas of Expertise

-  Women
-  Weight Management
-  Immune
-  Oral
-  Digestive
-  Brain

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