HOWARU® SHAPE
Feel like yourself while naturally keeping your waist trim
Worldwide obesity has more than doubled since 1980.¹

In 2016, more than 1.9 billion adults were overweight, and more than 650 million of those were classified as obese.²

**Obesity and overweight contribute to:**³
- Cardiovascular Disease
- Diabetes
- Joint Pain
- Cancer

Deaths caused by overweight and obesity³ 3.4 million

**HOWARU® Shape is here to help.**

Consumers continue to look for answers. Their search is the reason why the market for weight loss supplements has grown to an over $5 billion industry.⁴

This is why we created HOWARU® Shape, a probiotic formula that’s clinically proven to control waist circumference and body fat – particularly trunk fat. It’s also been shown to strengthen the good gut bacteria linked with metabolic health, which means the risk of weight-related health issues may be reduced.

**The benefits of maintaining a healthy weight go far beyond smaller clothing sizes.**

- More energy and greater ability to join in desired activities
- Fewer joint and muscle pains
- Better sleep patterns
- Better regulation of bodily fluids and blood pressure
- Reduced burden on your heart and circulatory system
- Reduced risk of developing Type 2 diabetes
- Reduced risk of heart diseases and certain cancers
HOWARU® Shape is clinically proven to keep waists trim – and benefit metabolic health

HOWARU® Shape is a unique formula of 10 billion CFU Bifidobacterium lactis B420™, available alone or in combination with 12g of the prebiotic fiber Litesse® Ultra™. Both formulas offer documented weight management benefits.

*Bifidobacterium lactis B420™ is a naturally occurring strain, originally isolated from dairy products. DuPont Nutrition & Health has studied the strain’s effect on metabolic health and the gut barrier function for more than a decade. In a recent study, the strain was found to increase the relative abundance of Akkermansia muciniphila in the gut microbiota – a bacterium linked with improved metabolic health and anti-inflammatory properties.

HOWARU® Shape does not contain stimulants and is proven safe, effective and well-tolerated. It is a highly stable product and ideal for capsules or sachets.

### Clinical results*

<table>
<thead>
<tr>
<th></th>
<th>B420™ **</th>
<th>B420™ + Litesse® Ultra™***</th>
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<tbody>
<tr>
<td>Has a weight management benefit</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Improved body composition</td>
<td></td>
<td></td>
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<tr>
<td>(fat/lean ratio)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controlled body fat mass</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Increased lean mass</td>
<td></td>
<td>●</td>
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<tr>
<td>Reduced energy intake</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Controlled trunk fat mass</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Controlled waist circumference</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Promotes short chain fatty acid (SCFA) production</td>
<td>●</td>
<td></td>
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<tr>
<td>Supports healthy microflora associated with metabolic health</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Promotes growth of beneficial bacteria</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Promotes an increase in Akkermansia which is linked to lean and healthy body weight</td>
<td>●</td>
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HOWARU® Shape is designed for the customer category “weight strugglers,” which represents 54% of the total market. This important audience is concerned about weight-related health issues, is motivated to diet, and wants an easy and effective weight-loss solution that helps them feel good about themselves. .

Weight strugglers are:

- Predominantly female
- Overweight or obese and are likely to have weight-related health issues
- Tired of going on diets to lose weight – they want a permanent solution

Weight strugglers feel guilty about not having a healthier diet. HOWARU® Shape offers a helping hand to support the weight management efforts of this target segment so they can take control of their health.

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* Structure/function claims are for your consideration only. Customers are fully responsible for the claims they choose to make.
** As compared to groups without B420
*** As compared to placebo
DuPont Nutrition & Health is a probiotic industry leader with a long history of scientific innovation. HOWARU® Shape is the new proven probiotic in the range.

HOWARU® Shape triples the chances of successful weight management when maintaining a regular lifestyle.

A double-blind, placebo-controlled study found that six months of dietary supplementation with the combination product resulted in:

- 4.5% less total body fat mass
- 6.7% less trunk fat
- 2.6 cm (1.02 inch) smaller waist circumference

Participants in the study made no other change to their diet or exercise regime.

The greatest benefits from B420™ + Litesse® Ultra™ are seen in the trunk region.

**Waist vs. hip area fat mass changes:**

- 4.7% less waist fat mass
- 1.6% less hip fat mass

* in subjects who followed the study protocol, compared to placebo.

Strong clinical documentation

*Bifidobacterium lactis* 420 (B420™) for metabolic health—a decade of research

<table>
<thead>
<tr>
<th>Year</th>
<th>Study Details</th>
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<tr>
<td>2007 - 2015</td>
<td>Cell culture studies: B420™ improves epithelial barrier function</td>
</tr>
<tr>
<td>2008 - 2013</td>
<td>Mouse studies: B420™ improves metabolic health and gut barrier function</td>
</tr>
<tr>
<td>2013 - 2016</td>
<td>Mouse studies: B420™ improves metabolic health and gut barrier function</td>
</tr>
<tr>
<td>2013 - 2016</td>
<td>MetSProb Clinical study: B420™ with or without Litesse® Ultra™ controls body fat mass</td>
</tr>
<tr>
<td>2017</td>
<td>MetSProb Clinical study: B420™ with or without Litesse® Ultra™ increases level of Akkermansia bacterium in the gut</td>
</tr>
</tbody>
</table>


Amar et al. EMBO Mol Med 2011

Garidou et al. Cell Metab 2015

Stenman et al. EBioMedicine 2016

Hibbert et al. Beneficial Microbes 2018


Stenman et al. Diabetol Metab Syndr 2015
Safe, proven effective formula

Why B420™?

Epithelial integrity is a key function of the gastrointestinal tract, and its disturbance is connected to metabolic disorders such as obesity. The finding of improved epithelial integrity by B420™ led to testing it for HOWARU® Shape. In mouse studies, B420™ was found to reduce weight gain and the accumulation of fat mass on an unhealthy diet. This provided first proof of concept of B420™ as an aid for weight management.

Why Litesse®?

Litesse® is a low calorie and water soluble fiber that is better tolerated than almost all other low caloric carbohydrates in commercial use (e.g. polyols, inulin). Clinical studies have shown Litesse® reduces energy intake at a subsequent meal and that energy was not compensated for later in the day (Hull et al 2012; Astbury et al 2013). It also reduced after-meal feelings of hunger, and increased GLP-1 response after meals, which is known to decrease food intake (Hull et al 2012; Olli et al 2015.)

Bicultobacterium lactis B420™ and Litesse® Ultra™ are documented as safe

B420™

- HOWARU® Shape contains Bicultobacterium lactis B420™, a fully documented B. lactis strain
- Bicultobacterium animalis ssp. lactis listed as QPS (Qualified Presumption of Safety) by EFSA
- The strain is not GM
- 16S rRNA and whole genome sequencing completed → facilitates registration
- Bile salt resistance & acid tolerance test completed → proven stability in GI tract conditions
- Minimum Inhibitory Concentration test completed → No evidence of transferable antibiotic resistance
- Biogenic amine productions test completed → No evidence of biogenic amine production
- No difference in reported adverse events between the study groups in the clinical study (Stenman et al. EBioMedicine 2016)

Litesse® Ultra™

- Generally approved for use in foods according to Good Manufacturing Practices (GMP)
- Approved food additive in the United States (21 CFR 172.841)
- Approved “Dietary fiber” in the United States (21 CFR 101.9(c)(6)(i))
  - Broad range of applications where polydextrose is permitted
  - Single serving exceeding 15 grams of Litesse® shall bear the statement: “Sensitive individuals may experience a laxative effect from excessive consumption of this product”
- Approved food additive in European Union (quantum satis)
- Additional function of ‘dietary fiber’ in over 30 countries worldwide
- Acceptable Daily Intake (ADI) ‘not specified’ allocated by JECFA
  - Laxation threshold ~ 90g per person per day or 50g as a single dose (Evaluation of certain additives. In: Thirty First Report of the Joint FAO/WHO Expert Committee on Food Additives, World Health Organization Technical Report Series 759, Geneva; 1987)
Another breakthrough from the probiotic category leader

HOWARU® Shape is the latest innovation in the premium line of DuPont™ Danisco® probiotics. Each of the HOWARU® probiotics are clinically-proven and designed to help users live their best lives.

A growing awareness of the relationship between diet and health has led to an increasing demand for food products and dietary supplements that enhance health as well as provide basic nutrition. Scientific studies have shown that ingestion of specific strains of friendly bacteria—probiotics—enhances several physiological functions, particularly the body’s natural defense system and intestinal well-being.

As with all DuPont Nutrition & Health products, our probiotics and fibers are manufactured to the highest quality standards and are tested rigorously to ensure safety and stability throughout their shelf life. DuPont is a world leader in applying market-driven science and innovation to solutions for the food, beverage and dietary supplement industries.

Other HOWARU® probiotics include Protect Adult, Protect Kids, Protect Senior, Protect Sport, Protect Early Life, Balance, Transit, Restore, and Dophilus.

References

4. Euromonitor International Jan 2017: Weight Loss Supplements Category
7. Stenman, Lotta K.; Lehtinen, Markus J.; Meland, Nils, Christensen, Jeffrey E., Yeung, Nicolas; Saarinen, Markku T.; Courney, Michael; Burcelin, Rémy; Lähdeaho, Manja-Leena; Linros, Juri; Apter, Dan; Scheinin, Mikko; Kloster Smerud, Hilde; Rissanen, Aila; Lehtinen, Sampo; Probiotic With or Without Fiber Controls Body Fat Mass, Associated With Serum Zonulin, in Overweight and Obese Adult Randomized Controlled Trial, EBioMedicine (2016; 13: 190-200), doi: 10.1016/j.ebiom.2016.10.036.