# BioDoph-3 GI™

## Targeted GI Intensive Probiotic

#### **Clinical Benefits\***

- · Clinically validated multi-species formula.
- Two randomized trials found benefit for participants with IBS, including improvements in indices related to quality of life and visceral hypersensitivity, as well as comfort and stool consistency.
- Shown to provide comfort to those with symptoms related to lactose intolerance.
- Likely mechanisms include promotion of gastrointestinal epithelial repair, modulation of microbiota and parasympathetic activity, inhibition of pathogenic species and inflammatory cytokines, and upregulation of SCFA production.
- Clinical trials all use the same dose, 3 × 10<sup>9</sup> cfus/capsule, given once per day.

### Strain Specific Benefits

**BioDoph-3 GI™** provides clinically validated probiotic strains at a dosage shown to be effective in randomized and controlled trials. Mediated via a combination of mechanisms that include immune modulation, secretion of anti-inflammatory exopolysaccharides, and enhanced epithelial regeneration, probiotics are widely recognized to promote intestinal barrier integrity and gut mucosal homeostasis.¹ Evidence has also emerged to support a much broader role for probiotics, not limited to gastrointestinal health. Crosstalk between gut microbiota and the liver demonstrate a role in liver health, for example, with gut-derived lipopolysaccharide (LPS) and short chain fatty acid (SCFA) production influencing liver injury and regeneration.² Probiotics also modulate the gut-brain axis, as evidenced by several clinical trials indicating improvements in sleep, feelings of anxiety and low mood.³-6

However, probiotic strain specificity as well as the combination effects of multi-species mixtures significantly influence their functional characteristics, requiring validation of efficacy for specific purposes. For example, it has been proposed that each strain may have a particular influence on the gastrointestinal tract, and that multi-species probiotics may have synergistic effects compared to isolated strains. Not every strain within a bacterial species has the same properties, i.e., *probiotic effects are strain specific*. For instance, in an animal study only one of four Bifidobacterium strains prevented diet-induced weight gain. A genomic analysis of 140 *Bifidobacterium bifidum* strains found many differences in strain-specific genes, which were associated with specific niches, indicating the importance of using specific strains with established functional effects.



BioDoph-3 GI™ available in a 30 capsule bottle (#1203)

# Clinical Trial Validation for Gastrointestinal Health

**BioDoph-3 GI™** contains two specific strains of *Lactobacillus plantarum* (KABP-022 and KABP-023) and *Pediococcus acidilactici* KABP-021 in a 1:1:1 ratio. In a double-blinded and randomized trial, it was shown to significantly improve IBS-related quality of life compared to placebo among participants meeting the Rome-III criteria for IBS-D.¹0 Additionally, it is the first multispecies probiotic to demonstrate improvement in the Visceral Sensitivity Index (VSI), a validated indicator of gastrointestinal symptom-specific anxiety.¹¹¹¹² Both a high and low dose were used, with no significant differences between them by the end of the trial, suggesting that the low dose (3 × 10° cfus/capsule given once daily) was as effective as a dose 5 times higher.

In a second randomized trial with three parallel arms, participants meeting Rome IV criteria for IBS (with diarrhea-predominant or mixed subtype) had significant improvements in quality of life, comfort levels, and stool consistency when given the same dosage of **BioDoph-3 GI™** compared to placebo, with even greater improvements when taken along with an antispasmodic.<sup>13</sup>

In an additional randomized and controlled trial, adult participants with lactose intolerance were given the same dosage of **BioDoph-3 GI™**. They had significant improvements in overall symptom scores compared to placebo, as well as sub-scores for abdominal comfort



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and flatulence.¹⁴ Lactose intolerance was confirmed by both subjective and objective assessments. Improvements were not only statistically significant, but also clinically meaningful; nearly half of those receiving the probiotic had reductions of 50% or more, compared to none of those receiving placebo. In agreement with the initial trial, this study also suggests (though it was not designed to determine) that **BioDoph-3 GI™** may support visceral comfort with hypersensitivity being a contributing factor to digestive symptoms (particularly after lactose ingestion) in sensitive populations.¹⁵

### Potential Mechanisms of Action

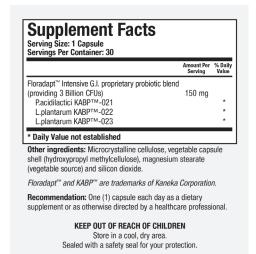
In vitro, the strains in **BioDoph-3 GI™** have been shown to produce the neurotransmitter acetylcholine, the SCFA acetate, antimicrobials against six IBS-specific bacterial strains, and polyphosphate (poly P), a repeated structure of phosphates which protects the intestinal cells from oxidative stress and inflammation and helps to maintain intestinal barrier integrity. 16-19 Acetylcholine has previously been linked to IBS; women with elevated serum cholinesterase activity were found to be twice as likely to be diagnosed with IBS-D.<sup>20</sup> Normally, the vagus nerve is the main regulator of the GI tract, and acetylcholine is the primary neurotransmitter of the parasympathetic nervous system. Acetylcholine binds to macrophages and inhibits the NFkB-mediated production of pro-inflammatory cytokines. Enhanced cholinesterase activity leads to more rapid degradation of acetylcholine, and inhibition of this anti-inflammatory pathway. Inhibition of vagal activity (and subsequent acetylcholine release) is the most likely pathway by which stress aggravates symptoms associated with IBS.<sup>21</sup> It also highlights a possible mechanism by which **BioDoph-3 GI™** may modulate the gut-brain axis; increasing the availability of acetylcholine may enhance parasympathetic activity and support healthy inflammation.

SCFAs are important to both intestinal and metabolic health; for example, animal studies suggest that restoration of acetate levels may underlie the protection Lactobacillus species provide against dietinduced metabolic syndrome.<sup>22</sup>

Additionally, in two animal models of colitis **BioDoph-3 GI™** demonstrated a protective effect, limiting the production of inflammatory cytokines IL-6 and IL-23, and inducing beneficial processes in the gut mucosa (none of these occurred with the VSL#3 multi-species probiotic).<sup>23</sup> It is likely that repair of the intestinal barrier is at least partly mediated by poly P production.<sup>24</sup>

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