# 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. 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. Probiotics also modulate the gut-brain axis, as evidenced by several clinical trials indicating improvements in sleep, feelings of anxiety and low mood. 34,5,6

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<sup>9</sup>



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. <sup>10</sup> Additionally, it is the first multispecies probiotic to demonstrate improvement in the Visceral Sensitivity Index (VSI), a validated indicator of gastrointestinal symptom-specific anxiety. <sup>11,12</sup> 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  $\times$  109 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 and flatulence.<sup>14</sup>



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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.<sup>15</sup>

### Potential Mechanisms of Action

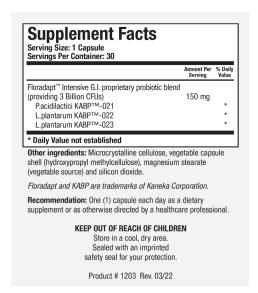
In vitro, the strains in BioDoph-3 GI have been shown to produce the neurotransmitter acetylcholine, the SCFA acetate, antimicrobials against six IBS-specific bacterial strains, and polyphosphate (poly P), a repeated structure of phosphates which protects the intestinal cells from oxidative stress and inflammation and helps to maintain intestinal barrier integrity. 16,17,18,19 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.21 It also highlights a possible mechanism by which BioDoph-3 GI may modulate the gutbrain 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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