



KEY POINTS

- ▶ Probiotics can be used in the management of a number of GI conditions.
- ▶ Probiotics can help alleviate antibiotic-associated GI signs.
- ▶ When selecting a probiotic, peer-reviewed studies proving efficacy are most important to consider.
- ▶ Evidence increasingly supports the use of probiotics for conditions such as anxiety and CKD, but proven safety and efficacy will remain critical as future uses are explored.

DEFINITIONS

- ▶ **Probiotics:** Live microorganisms that confer health benefits on the host when administered in adequate amounts.¹ Most probiotics are bacteria, but there is at least 1 yeast species (*Saccharomyces boulardii*) that qualifies as a probiotic as well.
- ▶ **Prebiotics:** Substrates that selectively promote the growth of microorganisms that confer health benefits²
- ▶ **Synbiotics:** A mixture of pro- and prebiotics

Gut Check

Pro- and synbiotics, which shift the host's microbiome and metabolome to achieve local and far-reaching effects,¹⁻² are being used increasingly to manage GI and extra-GI issues.³⁻⁸ This could reflect client demand for natural or alternative management modalities, intolerance of the adverse effects of conventional management, and/or failure of said management options to optimize patient outcomes.

Common Gastrointestinal Applications

Stress & Self-Limiting Gastroenteritis

Universal support of probiotics in managing stress-related GI signs has not been demonstrated. In adequately powered studies, pro/synbiotics decreased feline and canine diarrhea in shelter environments^{9,10}; however, similar efficacy was not demonstrated in weanling kittens,¹¹ working dogs under quarantine,¹² or racing Alaskan sled dogs, except during a week-long contagious outbreak.¹³

Impact on self-limiting gastroenteritis has been more consistently positive. Probiotics decreased the duration of self-limiting diarrhea, alone or with vomiting, by 32% to 41% as compared with controls in multiple randomized trials.¹⁴⁻¹⁷ Probiotics have also been found to significantly decrease hyporexia and vomiting,¹⁸ the use of rescue antibiotics,¹⁵ and study withdrawal for additional medical therapy such as antiemetics or antibiotics.¹⁶ In addition, resolution of acute diarrhea significantly correlated with probiotic administration and dietary modification, but not antibiotics, in a large observational study.⁸

Infectious Gastroenteritis

Probiotics may reduce the severity of clinical signs of infectious gastroenteritis, although adequately powered study results are limited. In a study, dogs with naturally occurring parvovirus enteritis were administered conventional therapy alone or in combination with a high-dose, multistrain probiotic cocktail.¹⁹ Dogs administered the probiotic were significantly less sick on days 3 and 5 of hospitalization and had lower mortality than dogs administered supportive care alone. Positive results also were identified for dogs with distemper virus-related diarrhea in a lower-quality trial.²⁰ Although clinical illness scores differed significantly from baseline 1 day earlier in dogs with acute hemorrhagic diarrhea syndrome given probiotics versus placebo, scores were not statistically significant between groups.²¹ Because scores were clinically equivalent and all dogs responded well to management, the benefit of probiotics in acute hemorrhagic diarrhea syndrome is questionable.

Non-Food-Responsive Chronic Enteropathy

Cats with idiopathic chronic enteropathy (CE) administered a multistrain synbiotic (Provia®-DC) had significantly lower fecal scores in an open-label trial.²² In another study, 9 out of 10 cats with idiopathic constipation/megacolon administered a high-dose probiotic had resolution of clinical signs, with clinically and statistically

significant histologic improvement.²³ Clinical activity scores were similarly improved in dogs with large-bowel dysmotility administered probiotics and a hydrolyzed, high-fiber diet.^{24,25} Clinical activity scores, defecation frequency, and fecal consistency also significantly improved in dogs with CE administered *S. boulardii* versus placebo in addition to conventional management,²⁶ as well as in dogs with colonic polyps given a high-dose multistrain bacterial probiotic.²⁷

Probiotics may also be useful for managing CE in dogs that fail to respond to diet change. In a study, clinical and histologic response rates did not differ for dogs treated with prednisone/metronidazole versus the same probiotic cocktail, with enhanced T regulatory cell function and dysbiosis normalization only in the probiotic group.²⁸ A follow-up study found no difference between dogs administered diet and prednisone alone as compared with the probiotic,²⁹ suggesting probiotic effects may be blunted by prednisone coadministration.

Antibiotic-Associated GI Signs

In the only study assessing the impact of probiotics on antibiotic-associated GI signs (AAGS) secondary to injectable antibiotic use, probiotic administration significantly decreased duration of lincomycin-induced diarrhea and inhibited it from developing when administered concurrently with the antibiotic.³⁰

With regard to oral antibiotics, in one feline study, administration of a probiotic 2 hours prior to administration of amoxicillin/clavulanate did not significantly decrease AAGS.³¹ In another study, coadministration of a synbiotic with clindamycin also did not decrease diarrhea in cats,³² although vomiting was less common in the synbiotic group. In a follow-up crossover study, administration of a higher-dose synbiotic (Provable®-Forte) 1 hour after clindamycin administration was associated with significantly increased food intake and decreased vomiting, and cats receiving the synbiotic were more likely to complete the initial

phase of the study.³³ This suggests that beneficial effects of the synbiotics persisted for ≥6 weeks after administration. Significant differences were also identified for food intake between the initial treatment period and after a 6-week washout, a phenomenon known as period effects (ie, when the washout between treatments is inadequate to prevent carryover effects from the initial treatment). In this case, food intake required to maintain weight was significantly higher at the start of period 2 for cats initially in the placebo group, which was consistent with development of antibiotic-induced CE. Several other placebo cats had persistent diarrhea at the end of the washout period, although period effects were not statistically confirmed. In another crossover study with an 8-week washout period, derangements in food intake were significantly lower for dogs that received a bacterial/yeast synbiotic combination (Provable®-Forte with Mycequin®) 1 hour after receiving enrofloxacin/metronidazole as compared with placebo.³⁴ Although vomiting and diarrhea did not statistically differ between groups, both were less severe during the second phase of the study; this suggests support for the synbiotic combination against AAGS. Significant differences in the microbiome and metabolome between groups were also found.^{2,32,35} Based on these results, administration of a synbiotic 1 to 2 hours after oral antibiotic administration has the highest likelihood of minimizing AAGS in cats and dogs.

Choosing a Probiotic

The most important criterion in product selection is demonstrated efficacy in peer-reviewed literature. Product species, microbial strains, and total microorganisms (colony-forming units) should be considered when scientific data are lacking.

Products containing more colony-forming units and microbial strains are recommended for the management of metabolic and GI disorders based on correlations between dose and efficacy

in humans.³⁶⁻³⁸ Yeast probiotics are not inactivated by antibiotics but can cause serious complications in immunocompromised patients. Products containing pre- and probiotics (ie, synbiotics) are often preferred for GI disorders because they act synergistically to support colonicocyte health. Animal protein flavorants can adversely impact patients with food sensitivity. Other selection considerations include administration and storage requirements. Because pro/synbiotics are not regulated as drugs in the United States and less than one-third of evaluated probiotics have been shown to meet or exceed the type and quantity of viable organisms listed on their labels,³⁹ only probiotics that undergo regular evaluations for content and viability should be used.

The Future of Probiotics

Probiotics rarely have adverse effects when appropriately administered, but an evidence-based approach to product selection and administration is essential for maximal benefits. Limited but moderate- to high-quality evidence supports pro/synbiotic administration for management of shelter-induced diarrhea, self-limiting gastroenteritis, parvovirus, intestinal dysmotility, and CE in cats and dogs. Several randomized, blinded placebo-controlled studies support the use of Provable®-Forte administered alone or in combination with Mycequin® (a yeast-based probiotic) to mitigate AAGS in patients receiving antibiotics. Evidence also increasingly supports the use of probiotics for some extra-GI issues such as anxiety and CKD.^{4,7} Results for other disorders such as canine atopy are mixed,^{3,5,6,40} with positive results found primarily in studies using probiotics with higher colony-forming units.^{3,5,6} This emphasizes the importance of careful product selection, administration, and attention to details of published research. ■

For references, please see
[cliniciansbrief.com/article/
clinical-notes-gut-check](https://cliniciansbrief.com/article/clinical-notes-gut-check)

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