

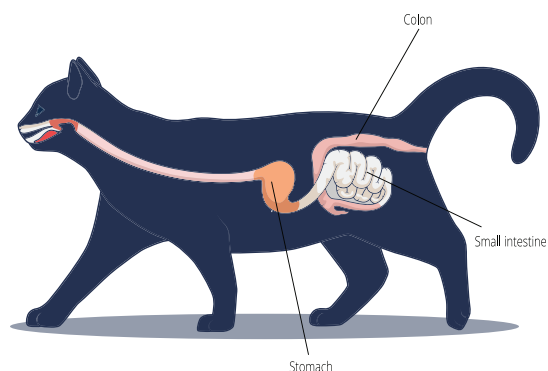
CLINICAL EVIDENCE REPORT

Hill's ActivBiome+ Technology Manages Microbiome Health in Dogs and Cats

The gastrointestinal tract is inhabited by communities of microorganisms essential to host health. These microorganisms are referred to as the microbiome and the exact population of microorganisms is unique to each host.

These bacteria are functionally and compositionally diverse, allowing contribution to energy homeostasis, metabolism, gut epithelial cell health, and immunologic activity; all of which ultimately are important for overall host health. Maintenance of this ecosystem is often desired even in healthy animals to optimize digestive benefits similar to how people are encouraged to eat their fruits and vegetables. This population is not static and can change due to medications such as antibiotics, environmental factors, disease states, and dietary influences. Additionally, it is common to see dysbiosis (imbalance in the gastrointestinal microbiome) in chronic GI disease in cats and dogs.

Over the past several years, Hill's has focused heavily on studying the microbiome, characterizing bacterial populations of the gastrointestinal tract of cats and dogs. Most critically, Hill's has performed analyses to understand the functions of those bacteria in the gastrointestinal tract.



Hill's has found that ActivBiome+ Technology, a unique blend of prebiotics, starts working quickly to activate each pet's unique gastrointestinal microbiome and release helpful postbiotics.



What is ActivBiome+ Technology?

Hill's ActivBiome+ Technology is a proprietary blend of prebiotics shown to rapidly activate the gut microbiome and release helpful postbiotics (metabolic products of microbial metabolism) to support digestive health and well-being. By promoting activity of beneficial gut bacteria, it also helps to suppress the growth of potentially undesirable bacteria and their metabolites. The prebiotic sources in ActivBiome+ Technology were

selected because they have multiple functions (such as water retention, stool bulking, and gastrointestinal transit) and contain fiber bound polyphenols. The microbes ferment the prebiotics and produce gut-nourishing compounds, as well as release and activate the aforementioned antioxidant and anti-inflammatory polyphenols. These and other postbiotics benefit the gut, as well as other organs and tissues.

How does ActivBiome+ Technology improve Gastrointestinal Health?

A series of studies at Hill's Pet Nutrition Center (PNC) were conducted demonstrating how ActivBiome+ Technology works and clinically showed improvements when this synergistic blend of prebiotics was added to certain foods. **Both dogs and cats showed improvements in markers of gastrointestinal microbiome health.**^{1,2} Dogs and cats also showed improvements in stool quality.²

One canine feeding study evaluated the benefits of the ActivBiome+ Technology in healthy dogs (n=16) and in dogs with chronic, recurrent enteritis or gastroenteritis (n=16) in a randomized, cross-over design study. ActivBiome+ Technology was added to either a hydrolyzed meat food (Food A, Fig 1) or grain-rich food (Food B, Fig 2) and fed over a 56 day period. **All dogs had significant improvements in stool quality, including those with chronic enteritis/gastroenteritis, when given food that included the ActivBiome+ Technology prebiotic blend.**²

ActivBiome+ Technology Improved Stool Quality in All Dogs

Fig 1

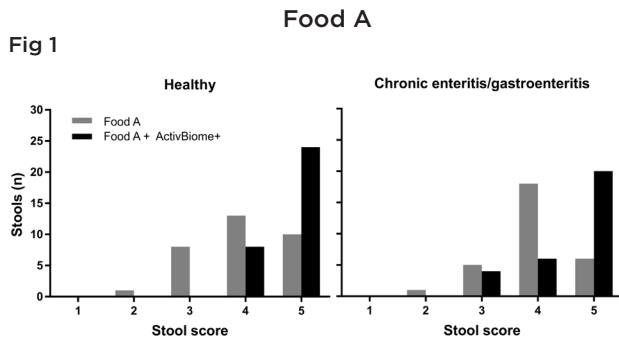
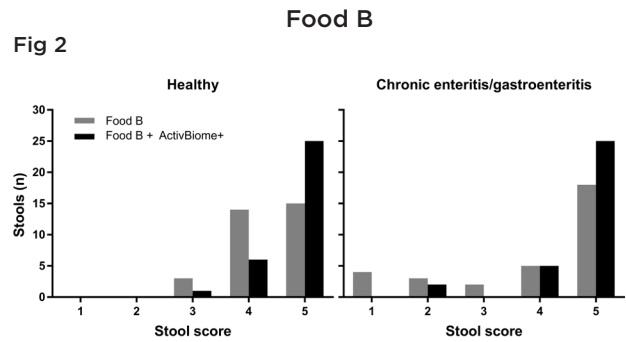


Fig 2



Figures 1 and 2 illustrate the changes in stool quality among all dogs consuming this prebiotic blend. By the end of 4 weeks, the stool quality score of the dogs with chronic enteritis/gastroenteritis had improved to the point that they were no longer significantly different from the healthy dogs.

Additionally, a significant increase in beneficial bacteria taxa (e.g. *Lachnospira* sp, Fig 3) and a decrease in harmful bacteria taxa (e.g. *Desulfovibrio* sp.) was observed. **This positive change in the microbiome also leads to an increase in the production of helpful postbiotics. ActivBiome+ Technology also significantly increased fecal levels of numerous other helpful postbiotics, including certain polyphenols and short-chain fatty acids (SCFA's).** The SCFA's help reduce fecal pH, creating an environment that favors the growth of beneficial bacteria in the host. Potentially harmful postbiotics (fecal polyamines such as putrescine, spermidine) were also measured and were reduced by the addition of ActivBiome+ Technology.²

ActivBiome+ Technology Shifts the Microbiome to a Healthier Balance

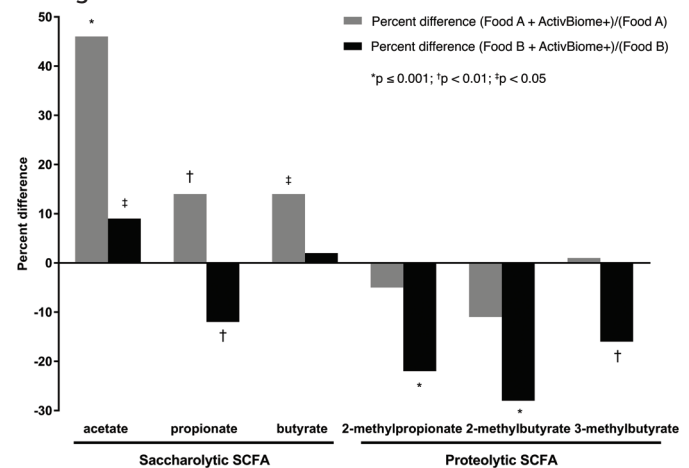
Fig 3

Genus	Food A		Food B	
	%Change w/ActivBiome+	p=	%Change w/ActivBiome+	p=
<i>Lachnospira</i>	↑ 330	0.001	↑ 285	0.001
<i>Desulfovibrio</i>	↓ 86	0.03	↓ 30	0.04

- ↑ Saccharolytic bacteria and those involved in polyphenol catabolism
- ↓ Some detrimental proteolytic bacteria or those involved in inflammatory activity

ActivBiome+ Technology Increases Healthy Short Chain Fatty Acids

Fig 4



Similar to dogs, the feline research done at the PNC on 28 healthy cats showed that ActivBiome+ Technology helped create a more positive gastrointestinal microbiome environment. There was a significant increase in beneficial bacteria. There was also a significant increase in key postbiotics such as SCFA's (acetic & propionic acids) from prebiotic fermentation and a decrease in fatty acids (isobutyric, 2-methylbutyric, & isovaleric acids) from protein breakdown (Fig 4). Increased stool moisture and decreased pH were also achieved while maintaining acceptable stool scores.¹



ActivBiome+ Technology is clinically proven to provide numerous benefits in both dogs and cats

- **Activate** – Activates the pet's individual gut microbiome & promotes a beneficial microflora
- **Release** – Releases & converts fiber bound polyphenols into more potent anti-inflammatory & antioxidant postbiotics
- **Increase** – Increases short-chain fatty acid production to nourish colonocytes
- **Balance** – Supports beneficial gut bacteria for a healthy gut microbiome balance
- **Promote** – Promotes healthy stool quality in healthy dogs & cats as well as dogs & cats with enteritis^{2,3,4}

¹Wernimont SM, Fritsch DA, Jackson M, et al. Specialized Dietary Fibers Alter Microbiome Composition & Promote Fermentative Metabolism in the Lower Gastrointestinal Tract of Healthy Adult Cats. *Current Developments in Nutrition*. 2019;3:20-45.
²Jackson M, Jewell DE. Balance of Saccharolysis and Proteolysis Underpins Improvements in Stool Quality Induced by Adding a Fiber Bundle Containing Bound Polyphenols to Either Hydrolyzed Meat or Grain-rich Foods. *Gut Microbes*. 2019;10(3):298-320.
³Wernimont SM, Fritsch DA, Jackson M, et al. Polyphenol-rich Dietary Fiber Sources Increased Antioxidant & Anti-inflammatory Polyphenols in the Lower Gastrointestinal Tracts of Healthy Adult Cats While Maintaining Fecal Characteristics Similar to Control. *FASEB J*. 2020;34(1):1.
⁴Wernimont SM, Fritsch DA, Schiefelbein HM, et al. Food with Specialized Dietary Fiber Sources Improves Clinical Outcomes in Adult Cats with Constipation or Diarrhea. *FASEB J*. 2020;34(1):1.
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