Healthy Holistic

BLUE

NATURAL

Veterinary Diet™

Enhanced with Vitamins, Minerals and Other Nutrients

VOLUME NO. 3

BLUE BUFFALO CLINICAL REPORT

Clinical Evidence for: GI Gastrointestinal Support

KEY POINTS

1. **BLUE Natural Veterinary Diet GI Gastrointestinal Support dry formulas resulted in a 23-24% quicker resolution of acute diarrhea in dogs and cats.**

2. **Multiple findings support that BLUE Natural Veterinary Diet GI provides an ideal approach for nutritionally managing pets with gastrointestinal conditions:**

- Rich in omega-3 fatty acids to help reduce inflammatory response of intestinal mucosal cells
- High digestibility for quick resolution of diarrhea
- Prebiotic and mixed fibers to nourish intestinal cells and support growth of beneficial bacteria

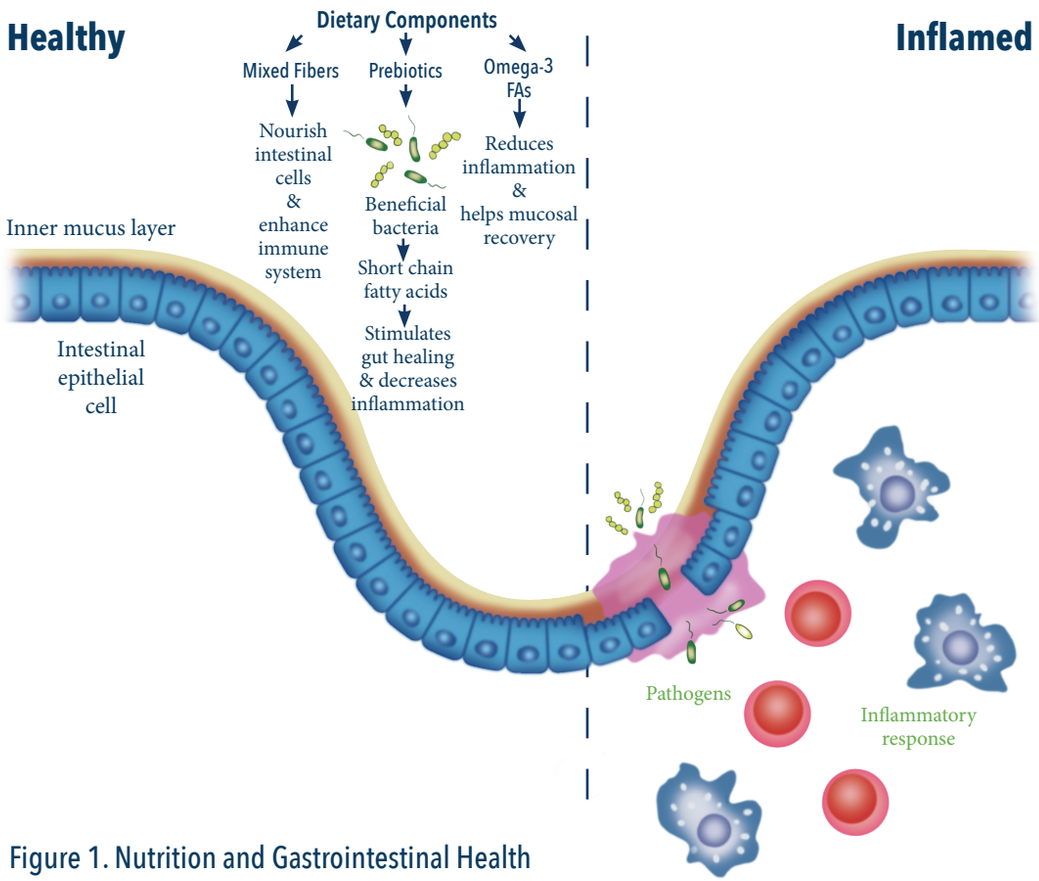


Figure 1. Nutrition and Gastrointestinal Health

BLUE Natural Veterinary Diet GI Gastrointestinal Support for Dogs and Cats

Gastrointestinal disease is a common reason for consultation in veterinary practice and can manifest in a variety of clinical symptoms. A number of acute and chronic enteropathies are recognized including gastritis, inflammatory bowel disease (IBD), protein-losing enteropathy, exocrine pancreatic insufficiency, colitis, pancreatitis and constipation. Currently, inflammatory bowel disease is considered the most common cause of chronic diarrhea and vomiting in dogs and cats.[1, 2] While the etiology of the disease may not be definitively identified in a particular case, the treatment and management of the condition typically revolves around eliminating the cause, controlling the symptoms and aiding the recovery of the gastrointestinal system. In addition to pharmacological and antimicrobial interventions, nutritional management has been clinically proven to help resolve and even control future relapses of gastrointestinal conditions.[3] Controlling inflammation associated with a disease is essential for successful outcomes and is a key aspect of nutritional management. Additionally, enhancing the functional ability of the organ systems to repair and restore to a healthy state is often where nutritional intervention can provide the most significant impact.

OPTIMAL NUTRITION TO MANAGE GASTROINTESTINAL CONDITIONS:

1) NUTRIENTS FOR A HEALTHY GI TRACT

Critically important aspects of managing gastrointestinal disease include short-chain fatty acids, mixed fiber sources and omega-3 fatty acids (See Figure 1). Short-chain fatty acids are the principal end-products of bacterial fermentation of dietary fibers and have profound effects on normal intestinal cell metabolism and proliferation. Short-chain fatty acids have the potential to improve overall intestinal health, stimulate intestinal healing, and decrease intestinal inflammation.[4] Mixed fiber sources help nourish intestinal cells and promote a balanced and healthy intestinal bacterial population, modify intestinal pH, enhance the immune system, and inhibit the growth of intestinal pathogens to promote optimal stools and reduce diarrhea.[5-8] Omega-3 fatty acids may also be useful to reduce intestinal immune cell damage and inflammation as well as protect against the damage of colitis.[9, 10] There is evidence that the gastrointestinal mucosa is highly responsive to long-chain polyunsaturated fatty acids such as omega-3s.[11] The intake of omega-3s can be helpful in the treatment of gastrointestinal conditions as it can alleviate the symptoms and help the recovery of the mucosa due to its anti-inflammatory properties.[12, 13]

STUDY: RESOLVING ACUTE DIARRHEA

PURPOSE

The following studies were conducted to show that feeding BLUE Natural Veterinary Diet GI Gastrointestinal Support dry diets can improve stool quality and speed the resolution of acute diarrhea in dogs and cats.

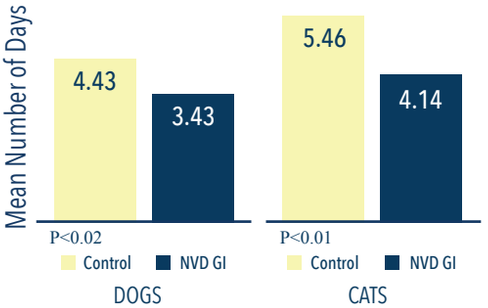
STUDY DESIGN

Dogs and cats older than 8 weeks that developed diarrhea on arrival at an animal shelter were fed either a species-appropriate control diet (leading dry pet food) or BLUE Natural Veterinary Diet GI dry food for 7 days in a randomized blind study. The Canine Acute Diarrhea Study included 23 dogs in the control group and 23 dogs in the BLUE Natural Veterinary Diet GI group. The Feline Acute Diarrhea Study included 32 cats in the control group and 32 cats in the BLUE Natural Veterinary Diet GI group. Animals selected were otherwise clinically healthy and both groups were managed in the same manner. Twice daily stool quality assessments including average daily scores and clean up characteristics were recorded. Stool samples were scored based on a numerical scale (1-7 scale, where 1 is firm and 7 is diarrhea). Stools were further characterized as "pick up" with a score 4 or less, and "wipe up" when the score was 5 or more. Time to resolution of diarrhea was determined for each animal as the number of days from day 0 (initiation of feeding) to achieving a stool score of 4 (ideal). Food intake and general health was assessed twice daily.

RESULTS[14, 15]

Dogs fed BLUE Natural Veterinary Diet GI dry food had mean time to diarrhea resolution of 3.43 days vs. 4.43 days for the control fed dogs, a 23% quicker resolution of diarrhea (P<0.02). Cats fed BLUE Natural Veterinary Diet GI dry food had mean time to diarrhea resolution of 4.14 days vs. 5.46 days for the control fed cats, a 24% quicker resolution of diarrhea (P<0.01). Results of monitoring general health, food intake, body weight, and blood variables were within normal ranges.

CHART 1. QUICKER RESOLUTION OF DIARRHEA



STUDY: IMPROVING CHRONIC DIARRHEA IN CATS WITH CHRONIC ENTEROPATHIES

PURPOSE

This study was conducted to show that feeding BLUE Natural Veterinary Diet GI Gastrointestinal Support dry diet can improve stool quality in cats with chronic diarrhea due to chronic enteropathy.

STUDY DESIGN

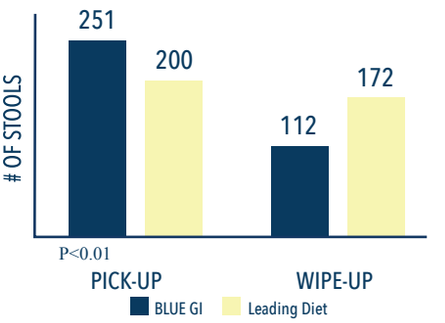
Twenty-two adult cats with clinical signs of chronic enteropathy including chronic diarrhea were recruited for a cross-over feeding study. These cats were residents of a commercial research facility. All cats were screened for pancreatic disease via assessment of fTLI (feline trypsin-like immunoreactivity) and fPLI (feline pancreatic lipase immunoreactivity)[16] at Texas A&M laboratory and 3 cats with elevated values were excluded. Nineteen cats were assigned to the treatment (BLUE Natural Veterinary Diet GI dry food) or control (leading dry cat food) diet phase for 28 days, then switched to the opposite diet phase, in a cross-over design. Food was offered once daily and available for 20 hours. No other treatments were administered during the study and both groups were managed in the same manner.

The following variables were evaluated during the study. Stool quality was assessed daily and an average stool score was determined for each cat. Stool samples were scored based on a 1 to 5 scale, with scores of 1 through 3 considered "pick up" and 4 through 5 considered "wipe up." Food intake was monitored daily and body weight weekly. Blood samples were analyzed on day 0 and at the end of each 28-day diet phase for: CBC, serum biochemistry, fTLI and fPLI, cobalamin and folate (day 0 only.)

RESULTS[17]

Cats with chronic diarrhea fed BLUE Natural Veterinary Diet GI dry food had significantly (P<0.01) more stools characterized as "pick up" and fewer stools characterized as "wipe up", compared with those fed the control diet.

CHART 2. IMPROVED STOOL QUALITY IN CATS WITH CHRONIC DIARRHEA



Healthy Holistic BLUE NATURAL Veterinary Diet Enhanced with Vitamins, Minerals and Other Nutrients

2) ENHANCED DIGESTIVE EFFICIENCY

Feeding highly digestible foods provides several advantages in the management of dogs and cats with gastroenteropathies.[1,2] Highly digestible foods are associated with reduced osmotic diarrhea, reduced production of intestinal gas and decreased antigen loads.[18, 19]

STUDY: NUTRIENT ANALYSIS AND DIGESTIBILITY

PURPOSE

To prove that BLUE Natural Veterinary Diet GI Gastrointestinal Support is a highly digestible food for both dogs and cats.

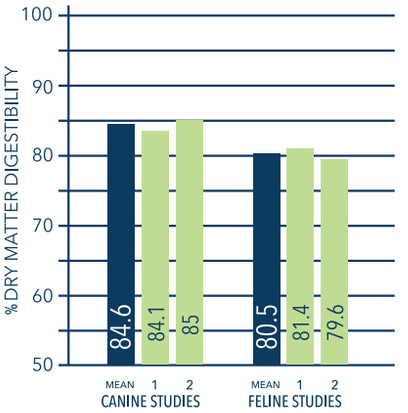
STUDY DESIGN

Two groups of adult dogs (n=6 each for Canine Digestibility Studies 1 and 2) and 2 groups of adult cats (n=7 each for Feline Digestibility Studies 1 and 2) from a commercial research facility were enrolled in the studies. All animals selected were clinically healthy. Animals were individually fed the species- appropriate BLUE Natural Veterinary Diet GI dry food once daily as their sole source of nutrition for 10 days. Animals were maintained individually in standard, species-appropriate housing and managed consistently during the study, including providing access to activity/exercise. Food consumption was monitored daily and body weights were recorded on days 1 through 6 and on day 10. On the last day of the study, a fecal sample from each animal as well as a sample of the BLUE Natural Veterinary Diet GI food was sent to a commercial laboratory for nutrient analysis. The results of these analyses were used to calculate digestibility values, including dry matter digestibility. Digestibility analysis was performed according to the recommended protocol for use in the determination of metabolizable energy of pet food as defined by AAFCO.[20]

RESULTS[21]

Mean results from two studies in each species showed that BLUE Natural Veterinary Diet GI dry food is highly digestible.

CHART 3. DIGESTIBILITY RESULTS



STUDY: DETERMINING STOOL QUALITY

PURPOSE

These 4 studies were conducted to show that feeding BLUE Natural Veterinary Diet GI Gastrointestinal Support dry formula can result in ideal stool quality (fecal consistency) in healthy dogs and cats.

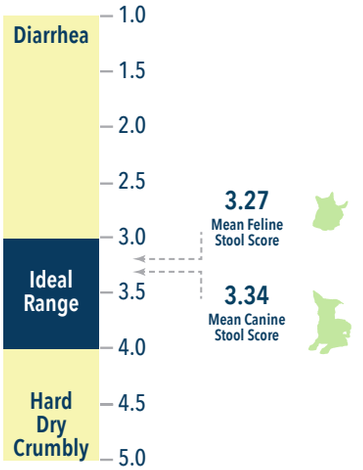
STUDY DESIGN

Two groups of adult dogs and 2 groups of adult cats (n=10 each for Canine Stool Quality Studies 1 and 2 and for Feline Stool Quality Studies 1 and 2) from a commercial research facility were enrolled in the studies. All animals selected were clinically healthy. Animals were individually fed the species-appropriate BLUE Natural Veterinary Diet GI dry food once daily as their sole source of nutrition for 7 days. For cats, food was made available over a 4-hour period. Animals were maintained individually in standard, species-appropriate housing and managed consistently during the study, including providing access to activity/exercise. Food consumption was monitored daily and body weights were recorded prior to study initiation and on study days 1, 3 and 5. Stool quality observations were made at least twice daily and scores were recorded. The scoring scale ranged from 1 for diarrhea to 5 for hard, dry crumbly feces and was aided by photographs of examples. In this study, a stool score between 3 and 4 is considered to represent ideal fecal consistency for dogs and cats.

RESULTS[21]

Overall, feeding BLUE Natural Veterinary Diet GI dry food in both dog and cat studies resulted primarily in moist, formed (score of 3) or well-formed, sticky (score of 3.5) stools.

FIGURE 2. STOOL QUALITY SCORING



3) SUPERIOR PALATABILITY[21]

Because of its impact on compliance and acceptability, high palatability is an important component of the nutritional approach to gastrointestinal conditions. Feeding studies in dogs and cats show that BLUE Natural Veterinary Diet GI Gastrointestinal Support is highly palatable.

STUDY: URINE RELATIVE SUPERSATURATION (RSS) EVALUATION

PURPOSE

To show that feeding BLUE Natural Veterinary Diet GI Support food can result in clinically significant urine RSS values for management of struvite and calcium oxalate urolithiasis.

STUDY DESIGN

Two groups of adult dogs (n=10 each for Canine RSS Studies 1 and 2) and 2 groups of adult cats (n=10 each for Feline RSS Studies 1 and 2) were enrolled in the studies. All animals selected were clinically healthy. Animals were maintained in standard, species-appropriate housing and managed consistently during the study, including providing access to activity/exercise. The study protocols were reviewed and approved by the research facility's institutional animal care and use committee.

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Animals were fed the species-appropriate Blue Natural Veterinary Diet GI Support food for 23 days. An amount of food calculated to maintain body weight was offered once daily and available for 1 hour for dogs and for 20 hours for cats. On day 22, a 24-hour urine sample was collected from each animal, using a metabolism cage with a urine collection system for dogs and a specialized litter box for cats. From that sample, urine pH was measured via pH meter and 2 aliquots were frozen and shipped to The University of Tennessee for RSS analysis.[22] Those aliquots included a 1-ml sample that was diluted with 1.5 ml 1N HCl, and a 10- to 15-ml sample placed in a sterile container. For the RSS analysis, urine sodium, potassium, chloride, calcium, magnesium, phosphorus, citrate, oxalate, ammonia, pH, creatinine, and uric acid were measured.

RESULTS[21]

The BLUE Natural Veterinary Diet GI Gastrointestinal Support canine dry formula has an RSS less than 1 for struvite uroliths (dissolution and prevention) and less than 10 for calcium oxalate uroliths (prevention). The BLUE Natural Veterinary Diet GI Gastrointestinal Support canine canned food has an RSS value less than 2.5 for struvite uroliths (prevention), and less than 10 for calcium oxalate uroliths (prevention). The BLUE Natural Veterinary Diet GI Gastrointestinal Support feline dry and canned diets have RSS values less than 1 for struvite uroliths (dissolution and prevention), and less than 10 for calcium oxalate uroliths (prevention).

STUDY: AAFCO FEEDING TRIALS[21]

FOR DOGS

Animal feeding tests using AAFCO procedures substantiate that Blue Natural Veterinary Diet GI Gastrointestinal Support for Dogs dry formulation provides complete and balanced nutrition for growth and maintenance, including growth of large size dogs (70 lbs. or more as an adult). BLUE Natural Veterinary Diet GI Gastrointestinal Support for Dogs wet formulation is formulated to meet the nutritional levels established by the AAFCO Dog Food Nutrient Profiles for all life stages, except for growth of large size dogs (70 lbs. or more as an adult).

FOR CATS

Animal feeding tests using AAFCO procedures substantiate that BLUE Natural Veterinary GI Gastrointestinal Support for Cats dry formulation provides complete and balanced nutrition for maintenance. BLUE Natural Veterinary Diet GI Gastrointestinal Support for Cats wet formulation is formulated to meet the nutritional levels established by the AAFCO Cat Food Nutrient Profiles for all life stages.

CLINICAL IMPACT

The results discussed in this Clinical Report, along with existing literature, provide evidence supporting the clinical efficacy, digestibility, stool quality and palatability for BLUE Natural Veterinary Diet GI Gastrointestinal Support for dogs and cats. These findings support that BLUE Natural Veterinary Diet GI Gastrointestinal Support for dogs and cats provides an ideal approach to nutritionally manage dogs and cats with a gastrointestinal condition, while satisfying pet owners' preferences for wholesome, natural diets.

For more information about Blue Buffalo Quality Assurance Testing and Clinical Research, please visit BLUEVetConnect.com or call 1-888-323-BLUE.