

## The use of SLAB51™ probiotics in dogs with acute and chronic gastrointestinal disease in a veterinary teaching hospital

*Het gebruik van SLAB51™-probiotica bij honden met acute en chronische maag-darmaandoeningen in een diergeneeskundig academisch ziekenhuis*

<sup>1</sup>T.W.J. Willemse, <sup>2</sup>S. Salavati Schmitz

<sup>1</sup>IVC Evidensia Small Animal Referral Hospital Hart van Brabant, 5144 AM Waalwijk, the Netherlands

<sup>2</sup>Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, the Roslin Institute, College of Medicine and Veterinary Medicine, University of Edinburgh, Easter Bush, Midlothian, EH25 9 RG, United Kingdom

Tijmen.willemse@gmail.com

### ABSTRACT

Acute and chronic gastrointestinal (GI) problems remain common conditions in dogs presented in primary and referral practice. For canine chronic enteropathies (CE), traditional treatment trials are being challenged. In particular, antibiotic use is increasingly scrutinized, and recommendations include replacement by probiotics. However, probiotic-responsive CE (PRE) is not well described yet. The authors hypothesize that this condition might exist and aimed to characterize these enteropathies and describe dogs that could fall into this category by retrospectively assessing response to probiotic treatment. Medical files of dogs receiving the most commonly used probiotic mixture at the authors' hospital, i.e. SLAB51™, were reviewed. Information about signalment, presenting signs, diagnosis, concurrent treatment, length of treatment and outcome was collected. Dogs with chronic disease supplemented with SLAB51™ (either alone or concurrently to other treatments) were further described to identify cases of PRE. Thirty-seven dogs met the inclusion criteria, of which 29 had chronic GI signs and 24 dogs had a CE. Seven of eight dogs in the acute group and 18/29 dogs in the chronic group responded favorably to treatment. Seven dogs received SLAB51™ without significant concurrent treatment, out of which six had a favorable response (two partial and four full resolution of clinical signs). While the number of cases in which the response to probiotics alone could be assessed, was small, in this study, a role for the use of SLAB51™ probiotics is suggested in cases of acute and chronic enteropathies either alone or alongside other management changes such as dietary interventions.

### SAMENVATTING

Acute en chronische gastro-intestinale (GI) aandoeningen blijven veelvoorkomende problemen bij honden in de eerstelijns- en verwijspraktijk. Voor chronische enteropathieën (CE) bij honden wordt de traditionele behandelingsmethodiek tegenwoordig in twijfel getrokken. Vooral het gebruik van antibiotica wordt bekritiseerd en er wordt onder andere aanbevolen het gebruik daarvan te vervangen door het gebruik van probiotica. Echter, probiotica-responsieve CE (PRE) zijn niet goed beschreven. De auteurs vermoeden het bestaan van deze enteropathieën en probeerden deze aandoeningen en de honden die vermoedelijk aan deze aandoeningen lijden, te beschrijven door de respons op behandeling met probiotica retrospectief te beoordelen. De medische dossiers van honden die het meest gebruikte mengsel van probiotica (SLAB51™) in het Royal (Dick) School for Veterinary Sciences' Hospital for Small Animals kregen, werden doorgenomen. Informatie over signalement, symptomen, diagnose, gelijktijdige behandeling, duur van de behandeling en het resultaat werd verzameld. Honden met chronische GI-aandoeningen die SLAB 51™ toegediend kregen (alleen of gelijktijdig met andere behan-

delingen) werden verder beschreven om gevallen van PRE te identificeren. Zevenendertig honden voldeden aan de inclusiecriteria, waarvan 29 honden chronische GI-klachten hadden en 24 honden aan een CE leden. Zeven van acht honden in de groep lijdend aan acute enteropathieën en 18/29 honden in de groep met chronische maagdarmklachten reageerden positief op de behandeling. Zeven honden kregen SLAB51™ zonder relevante veranderingen van de gelijktijdige behandeling, waarvan er zes een gunstige respons hadden (twee gedeeltelijke en vier volledig verholpen van klinische symptomen). Hoewel het aantal gevallen waarbij de respons op probiotica alleen kon worden beoordeeld, klein was, wordt in deze studie gesuggereerd dat het gebruik van SLAB51™-probiotica een rol kan spelen bij de behandeling van acute en chronische enteropathieën, alleen of simultaan naast andere behandelingen zoals diëtaire interventies.

## INTRODUCTION

Gastrointestinal (GI) clinical signs like vomiting, nausea, diarrhea and weight loss are frequent reasons for dogs and cats to be presented in veterinary practice. In fact, these problems make up between 9.4-17.8% of the consultations in both first-opinion and referral practices (Dandrieux and Mansfield, 2019). Chronic enteropathy (CE) is defined as a GI disease ongoing for more than three weeks for which no obvious cause (infectious, neoplastic, extra-GI) can be found. Often, CE is confirmed by the presence of inflammatory infiltrates of the GI mucosa to various degrees, and has to be differentiated from diffuse neoplasia-like GI lymphoma. The prevalence of CE is suggested to be about 1-2% in referral populations (Kathrani, 2011; Marchesi et al., 2017). Subtypes of CE include food-responsive enteropathy (FRE), antibiotic-responsive enteropathy (ARE), immunosuppressant responsive enteropathy (IRE) and non-responsive enteropathy (NRE) (Dandrieux, 2016; Dandrieux and Mansfield, 2019; Jergens and Heilmann, 2022).

In recent times, the routine use of antibiotics in small animals with GI disease is increasingly scrutinized. Whilst ARE is well described in dogs, and likely overlapping with the descriptive diagnosis of small intestinal bacterial overgrowth (SIBO) in the older literature, most dogs relapse quickly after the antibiotic is discontinued (Dandrieux and Mansfield, 2019), suggesting that treatment isn't curative. Long-term use of antibiotics is even more problematic, particularly in the context of worldwide rising antimicrobial resistance (Dandrieux and Mansfield, 2019, Jergens and Heilmann, 2022). There is also robust evidence that the antibiotics most commonly used in small animal CE, namely metronidazole and tylosin, cause dramatic dysbiosis of the intestinal microbiota, in both healthy and diseased animals - in some individuals with long-term detrimental effects (Jergens and Heilmann, 2022; Stavroulaki et al., 2023). While simply 'leaving out' the sequential treatment with antibiotics for CE is possible, treatment with immunosuppressive drugs as the next available measure also comes with significant drawbacks: many dogs develop intolerable side effects, and long-term outcomes are highly variable, with up to 50% of dogs with IRE

relapsing (Marchesi et al., 2017). Because of these challenges in treating CE, there is a real need for additional and alternative treatment options.

There are a number of studies assessing probiotics as potential treatment for CE that could fulfill this requirement. Probiotics are defined by the WHO as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" (Joint FAO/WHO Expert Consultation, 2001; Hill et al., 2014). Several purported mechanisms have been reported, including direct competition with pathogenic microorganisms (Collado et al., 2007; Lee et al., 2023), production of antimicrobial substances (Jones and Versalovic, 2009), immunomodulation within the mucosa (Castagliuolo et al., 1999; Medellin-Pena, 2007; Pagnini et al., 2010, Schmitz et al. 2013; Schmitz et al., 2014) and improvement of intestinal barrier function by increasing the expression of tight junction proteins (Ramezani Ahmadi et al., 2020; di Vito et al., 2022). Probiotics have been used in humans to treat or prevent various conditions, including Crohn's disease, acute diarrhea in children and antibiotic-associated diarrhea (Blaabjerg et al., 2017; Huang et al., 2021; Vakadaris et al., 2023). Meta-analyses of the latter linked the use of probiotics to a decrease in diarrhea by 51%, and found a decrease in duration of diarrhea and length of hospitalization in diarrheic children when treated with probiotics (Blaabjerg et al., 2017; Huang et al., 2021). In a recent systematic review by Vakadaris et al. (2023), 21/25 studies were found to show a positive effect of the administration of probiotics in humans with Crohn's disease.

A probiotic blend called SLAB51™ (Table 1) is currently promoted for the veterinary market, and there are studies supporting its use in acute hemorrhagic diarrhea syndrome (AHDS) (Ziese et al., 2023), irritable bowel syndrome (Rossi et al., 2020) and parvoviral enteritis in dogs (Arslan et al., 2012), as well as constipation in cats (Rossi et al., 2018). Some of the bacteria in this blend have been studied as probiotics before, with both *Bifidobacterium* strains and *Lactobacillus* strains reducing the time to normal fecal consistency in dogs with idiopathic acute diarrhea (Strompfová et al., 2008; Kelley et al., 2009).

SLAB51™ has not been assessed extensively for its use in 'uncomplicated' acute gastroenteritis/ idiopathic diarrhea in dogs nor in dogs with CE, but has

**Table 1. Comparative composition of two commonly used probiotic blends in dogs and cats.**

The Simone formulation (VSL#3 until 2016, Visbiome® or Vivomixx® after 2016)	SLAB51™ (Sivoy® until 2018, Sivomixx® after 2018)
<i>L. acidophilus</i> DSM24735	<i>L. acidophilus</i> DSM32241
<i>L. plantarum</i> DSM24730	<i>L. plantarum</i> DSM32244
<i>L. paracasei</i> DSM24733	<i>L. paracasei</i> DSM32243
<i>L. delbrueckii</i> subspecies <i>bulgaricus</i> DSM24734	<i>L. helveticus</i> DSM32242
<i>B. longum</i> DSM24736	<i>L. brevis</i> DSM27961
<i>B. infantis</i> DSM24737	<i>B. lactis</i> DSM32246
<i>B. breve</i> DSM24732	<i>B. lactis</i> DSM32247
<i>Streptococcus thermophilus</i> DSM24731	<i>Streptococcus salivarius</i> subspecies <i>thermophilus</i> DSM32245

B: bifidobacterium, DSM: German collection of microorganisms, L: lactobacillus.

been used empirically, for example in situations where the previously studied probiotics were not available, as their composition is very similar to this probiotic blend (Table 1).

The aim of this study was to describe the empirical use of the SLAB51™ blend in a veterinary teaching hospital with the hypothesis that it would be effective in treating acute and chronic GI conditions. Specifically, it was aimed to describe the frequency of its use, indications, ancillary treatments and the clinical outcome in dogs that were prescribed this probiotic mixture. A secondary objective was to identify a subpopulation of dogs with CE that could be responsive to probiotic treatment alone, and hence possibly represent a new ‘type’ of CE termed probiotic-responsive enteropathy (PRE).

## MATERIAL AND METHODS

### Cases

Electronic patient records of the hospital’s primary and referral cases from December 2018 to February 2020 were searched for dogs that had been prescribed products containing the SLAB51™ blend (e.g. Sivomixx® or Sivoy®).

Only dogs that were given SLAB51™ for  $\geq$  five consecutive days were included. Additional inclusion criteria were the availability of a final or descriptive diagnosis relating to the GI tract, and the availability of information from at least one follow-up visit either via a phone conversation, a subsequent visit or through the referring veterinarian. Exclusion criteria were dogs that had GI signs due to diseases outside of the GI tract.

Initial diagnoses based on the electronic patient files (Veterinary Nomenclature or Venom codes) were reviewed by re-assessment of individual case data and follow-up information. Based on this, the cases were divided into dogs with acute (group A) or chronic GI signs (group C). GI signs were defined as having clinical signs including but not limited to vomiting, nausea, diarrhea and weight loss, and chronic was defined in this context as having clinical signs for longer than three weeks. Group C was divided into dogs with CE (further subclassified as FRE, ARE and IRE where possible), protein-losing enteropathy (PLE), GI neoplasia and miscellaneous chronic GI diseases based on the response to various therapies, serum albumin concentrations and histopathological diagnosis where possible.

Treatments administered in addition to probiotics for both groups A and C were broadly divided into dietary and medical interventions. The latter were further classified as antimicrobials, immunosuppressants, supportive GI drugs (such as antiemetics or gastric protectants), analgesics and others.

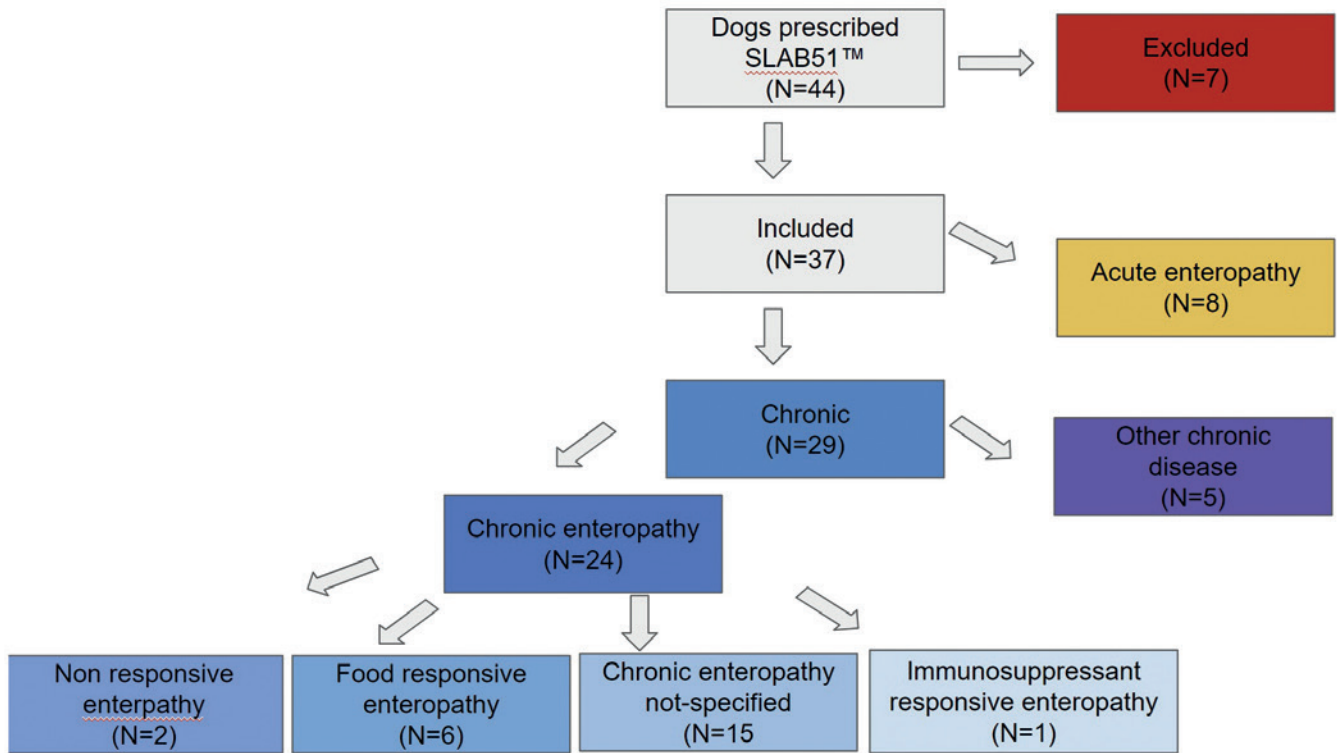
Outcome was defined as deceased (O1; regardless of cause of death), clinical signs either failing to improve or worsening (O2; partial response / O3; improvement of clinical signs) or full response (O4; complete resolution of clinical signs).

Dogs with PRE were defined as cases that showed clinical improvement when little to no changes were made in medical or dietary management, except for the addition of SLAB51™. Dogs were still considered as most likely having PRE when they only received consecutive antiparasitic treatment, when drugs were discontinued that did not lead to improvement of clinical signs and when changes between different hydrolyzed diets were made.

## RESULTS

Thirty-eight cases fulfilled the inclusion criteria. One dog received SLAB51™ probiotics for hemorrhagic diarrhea most likely due to underlying immune mediated thrombocytopenia, and was also excluded. In the end, 37 dogs were included in the study, of which eight (21.6%) were in group A and 29 (78.4%) in group C (Figure 1).

Group A consisted of six female neutered dogs



**Figure 1.** Flow chart of the distribution and classification of dogs who were prescribed SLAB51™ probiotics. N: number of cases.

**Table 2.** Diagnosis, signalment, concurrent treatment, length of probiotic administration and response in eight dogs with acute gastrointestinal signs treated with SLAB51™ probiotics. Medication given for concurrent, non-gastrointestinal disease is written in *Italics*.

Case	Signalment	Diagnosis	Concurrent treatment	Length of treatment	Response
1	8y0m, FN, Labrador	Drug induced gastroenteritis	Calcium- aluminosillicite clay, <i>prednisolone</i> , ranitidine, chlorphenamine	15 days	Resolved
2	7y6m, FN, Labrador	AHDS, IMHA	<i>Prednisolone</i> , <i>azathioprin</i> , <i>clopidogrel</i>	5 days	Died
3	6y8m MN, Cocker spaniel	Drug induced gastroenteritis, IMHA	<i>Prednisolone</i> , <i>cyclosporine</i> , amoxicillin, <i>mycophenolate</i> , tylosin	30 days	Resolved
4	4y1m FN, dandie dinmont terrier	Acute postoperative enterocolitis after spinal surgery	Kaolin, <i>E. faecium</i> , montmorillonite, metoclopramide, omeprazole	6 days	Improved
5	10y10m, FN, Lurcher	AHDS	Fenbendazole, omeprazole, sucralfate	5 days	Resolved
6	4y2m, FN, toy poodle	AHDS	Gabapentin, omeprazole, maropitant	7 days	Resolved
7	3y10m, FN Vizsla	Chemotherapy induced gastroenteritis	Maropitant	7 days	Resolved
8	3y0m, MN Dachshund	Acute postoperative enterocolitis	Maropitant, pantoprazole, <i>robenacoxib</i>	5 days	Resolved

AHDS: acute hemorrhagic diarrhea syndrome, IMHA: immune mediated hemolytic anemia.



and two male neutered dogs with a median age of 65 months (range: 36 to 130 months). The only breed represented more than once was the Labrador retriever (2/8); all further breed information can be found in Table 2. The main presenting complaints alongside acute diarrhea (n=8/8) were hematochezia (3/8) and acute vomiting (2/8). Individual case information including the final diagnoses and ancillary treatments (for both GI and concurrent diseases) can be found in Table 2. Two of the included dogs (dogs 2 and 3) also had immune-mediated hemolytic anemia (IMHA), one dog (dog 1) received prednisolone for a mast cell tumor and one dog (dog 7) developed acute drug-induced gastroenteritis during a course of chemotherapy for multicentric lymphoma. In six dogs of group A, GI signs resolved within a median of seven days (range 5 to 15 days), in one dog (dog 4), the clinical signs improved, but had not completely resolved at the time of the last follow-up (day 5). The remaining dog (dog 2) died before discharge of complications of the underlying condition, IMHA (Table 2).

Of the 29 dogs in group C, eleven (37.9%) dogs were female neutered, eleven (37.9%) male neutered, five (17.2%) male entire, one (3.4%) female entire, and one female dog was of unknown neuter status. The median age in this group was 56 months (range: 2 to 184 months). Breeds represented by more than one dog were crossbreeds (n = 5; 17.2%), Labrador retrievers (n = 4; 13.8%), greyhounds (n = 3; 10.3%), whippets (n=2; 6.9%) and cocker spaniels (n = 2; 6.9%) and one each of Bichon Frise, cavalier King Charles spaniel, Tibetan terrier, boxer, French bulldog, German shepherd dog, Border collie, Scottish collie, Jack Russell terrier, Miniature Schnauzer, West Highland white terrier, Border terrier, Shih Tzu.

Twenty-four dogs in group C (82.7%) were diagnosed with CE. Of these, six (20.7%) were classified as FRE, one as IRE and two as NRE, one of which responded to fecal microbiota transplantation (FMT). Of the remaining 15 (69.0%) dogs with CE, ten had not responded to any therapy at the last recorded visit. Two dogs with CE had additional diagnoses: one dog had concurrent chronic pancreatitis and one had mesenteric pyogranulomatous lymphadenitis. Three dogs in group C were diagnosed with PLE, of which one was classified as secondary to CE, and for this purpose was included in the CE group. Of the three remaining dogs in group C, one (3.4%) had a final diagnosis of primary GI lymphoma, one (3.4%) was diagnosed with ulcerative colitis, whereas in the other dog (originally presented for pica), no final diagnosis was made and pica remained the working diagnosis.

Treatments and therapeutic diets prescribed concurrently with SLAB51™ to the 24 dogs diagnosed with CE in relation to their GI signs are listed in Table 3; this includes drugs that had been started before treatment with SLAB51™ probiotics was started and were continued as well as new drugs that were started at the same time. The most commonly concurrent

**Table 3. Concurrent treatment for gastrointestinal signs in dogs diagnosed with chronic enteropathies treated with SLAB51™ probiotics.**

<b>Chronic enteropathy (non-classified, IRE, NRE) (18 cases)</b>	
<b>Medical therapy</b>	<b>Number of cases treated</b>
Antibacterials	4
Immunosuppressants	7
Anti-emetics, gastroprotectants, antidiarrheals	10
Analgesics	3
Miscellaneous	6
<b>Diet</b>	16
Hydrolyzed	7
Easily digestible	3
Low fat	4
Unspecified/homecooked	2
<b>Food Responsive Chronic Enteropathy (6 cases)</b>	
<b>Medical therapy</b>	<b>Number of cases treated</b>
Antibacterials	0
Immunosuppressants	0
Anti-emetics, gastroprotectants, antidiarrheals	1
Analgesics	0
Miscellaneous	2
<b>Diet</b>	6
Hydrolyzed	6
Easily digestible	0
Low fat	0
Unspecified	0

CE: chronic enteropathy, FRE: food responsive enteropathy, IRE: immunosuppressant responsive enteropathy, NRE: non-responsive enteropathy.

treatment was a diet (all six dogs with FRE and 16/18 of the dogs with other types of CE). All dogs diagnosed with FRE were given a hydrolysed diet, 7/18 (38.9%) dogs with other types of CE were given a hydrolysed diet, 4/18 (22.2%) a commercial low-fat diet, 3/18 (16.7%) a restricted protein easy-to-digest diet, and two (11.1%) had an unspecified home-cooked diet. Concurrent medications given were maropitant and prednisolone, both prescribed in seven (29.2%) cases, fenbendazole and cobalamin, both used in five (20.4%) cases and omeprazole in four cases (16.6%). At the end of the follow-up period, 3/29 dogs in group C were deceased (10.3%; NRE =2, lymphoma =1). In terms of response to SLAB51™ supplementation, 8/29 (27.6%) showed no improvement, 8/29 (27.6%) showed partial improvement and 10/29 (34.5%) showed complete resolution of clinical signs.

In 22/29 dogs from group C (75.9%), SLAB51™ probiotics were given alongside other treatment

**Table 4. Description of signalment, final diagnosis, previous and concurrent treatments of dogs with chronic gastrointestinal signs responsive to SLAB51™ probiotics. Previous treatment denotes any treatment that was given before SLAB51™ probiotics were given, concurrent treatment denotes any treatment modalities given at the same time as the SLAB51™ probiotics. A \* denotes no final diagnosis was made. Any diet in italics marks a case where a change in hydrolyzed diet to that of another brand was made.**

Signalment	Presenting complaints	Diagnosis	Previous treatment	Concurrent treatment	Duration of probiotics	Outcome
13y3m, MN Border terrier	Pica, lethargy, hyporexia, weight loss	Pica*	Metronidazole	-	20 days	Resolved
9m, ME, Cocker spaniel	Intermittent diarrhea	FRE, persistent Giardiasis	Hydrolyzed diet	<i>Hydrolyzed diet</i>	38 days	Resolved
1y8m, ME, Labrador	Flare-ups with small intestinal diarrhea, weight loss	CE	Low fat diet, Kaolin	Low fat diet	60 days	No improvement
10y1m, F, X-breed	Inappetence, flatus, hematochezia, large intestinal diarrhea	CE, chronic pancreatitis	Prednisolone, paracetamol, hydrolyzed diet	Prednisolone, paracetamol, hydrolyzed diet	30 days	Resolved
5y0m, FN, Lab	Chronic regurgitation	CE	Hydrolyzed diet, omeprazole	Hydrolyzed diet	44 days	Resolved
15y4m, FN, Border terrier	Intermittent vomiting and diarrhea	CE	Pancreatic enzymes, vitamin B12, mirtazapine	Vitamin B12	10 days	Improved
2y9m, MN,	Weight loss	CE	Hydrolyzed diet	<i>Hydrolyzed diet</i>	14 days	Improved

CE: chronic enteropathy, FRE: food responsive enteropathy.

changes, while in 7/29 (24.1%), SLAB51™ supplementation was given with other minimal management changes. They consisted of two neutered male dogs, two entire male dogs, two spayed female dogs and one entire female dog. The median age of this group was sixty months (range 9 to 184 months). The clinical signs were diarrhea in four dogs, weight loss in three dogs, and hyporexia in two dogs. Pica, vomiting, regurgitation, flatus, hematochezia, regurgitation and lethargy were all described once in this subgroup. Details of this group are summarized in Table 4.

In 4/7 of dogs with potential PRE, other medications were discontinued at the time of introducing probiotics, as they weren't deemed to improve or resolve clinical signs. One of these seven dogs did not have any concurrent treatment. Four also received a hypoallergenic diet and one a low fat diet. In 2/7 dogs, a change in the type of hydrolyzed prescription diet was performed at the time the probiotics were introduced. In one dog, SLAB51™ was started during an ongoing course of vitamin B12 supplementation. The remaining dog had no change in treatment when SLAB51™ was started. This dog had progressively worsening flare-ups consisting of inappetence, flatus, hematochezia, and large intestinal diarrhea whilst being treated chronically with a low dose of prednisolone, paracetamol and a hydrolyzed diet. After thirty days of treatment with SLAB51™, the clinical signs resolved.

With probiotic treatment, the clinical signs resolved in 4/7 cases, improved in 2/7 cases and did not improve in one dog. Based on this, six cases could be classified as fully or partially PRE. Full case details are given in Table 4.

Based on this, six cases could be classified as fully or partially PRE. Full case details are given in Table 4.

## DISCUSSION

To the authors' knowledge, this study is the first to attempt assessing the clinical efficacy of using the probiotic blend SLAB51™ in the context of 'uncomplicated' acute GI disease and chronic GI disease in dogs from a mixed hospital population.

The results revealed that SLAB51™ was only used in a small amount of cases with acute GI disease, probably reflecting that this is only a small patient group in a referral hospital. All dogs in the group suffering from acute enteropathies recovered except for one, who died because of comorbidities. It is difficult to interpret this result by itself, as there were only a small number of dogs in this group and as many of the diseases diagnosed in this group are usually self-limit-

ing. There are studies in companion animals that support the use of *Enterococcus faecium* (EF), a different probiotic, particularly in acute and uncomplicated GI signs in dogs. In one of these studies, the administration of an EF containing synbiotic (a combination of probiotics with prebiotic fibres) reduced the time compared to a placebo until resolution of diarrhea and the need for additional therapy in dogs with acute diarrhea (Nixon et al., 2019). However, in two recent systematic reviews, it has been shown that for the treatment and prevention of acute GI disease, other probiotics have a limited and possibly clinically negligible effect (Jensen and Bjørnvad, 2019; Scahill et al., 2024). The findings in the current study should be interpreted through this lens, and further prospective studies with a control group on the use of SLAB51™ in dogs with acute GI disease are necessary.

In an earlier study, the use of the probiotic ‘de Simone formulation’ (DSF), which is a mixture of seven different lactic acid bacteria (LABs) detailed in Table 1, has been shown to be equally effective in reducing clinical signs in dogs with CE compared to the control treatment consisting of a combination of prednisolone and metronidazole (Rossi et al., 2014). For dogs with CE, SLAB51™ has been rarely prescribed as a sole form of treatment, but rather as an adjunctive to other management modalities, mostly dietary modifications, but also prednisolone, maropitant, fenbendazole and cobalamin. This mirrors both the multifaceted nature of CE pathogenesis and the current treatment algorithm for these patients. Seven dogs were identified in which the effect of adding SLAB51™ to their treatment could be evaluated on its own or aside from minimal other changes in their treatment plan. Four of these dogs had complete resolution of their clinical signs, which would potentially represent a new subgroup of CE (PRE), while two dogs showed some improvement, making them partially fulfill criteria for PRE. The dogs with potential PRE had not responded to other treatments before and did not have a final subtype of CE captured as diagnosis on their patient file, further suggesting that they did not fit the other ‘typical’ categories, like FRE or IRE. However, due to the retrospective nature of this study, it was impossible to rule out that the minimal changes in treatment influenced the response of these dogs. Additionally, any treatment changes that occurred without the authors’ knowledge, could have influenced the response in those dogs, or any of the other dogs in this study.

This study was not set up to make recommendations about the cases in which these probiotics are indicated. The retrospective nature of the study introduces challenges like the frequent concurrent treatment and variations in work-up leading to heterogeneity of diagnoses. A prospective standardized protocol including a control group would allow for a better assessment of the sole effect of probiotics in GI diseases, like CE, and is necessary to prove that PRE exists as a defined disease entity. Standardized follow-up visits and clinical severity scoring using a system like the

canine IBD activity index (CIBDAI) would have allowed more objective assessment of clinical severity, but was also not consistently performed.

However, descriptive studies, such as the present, mapping the current use of probiotics, are useful to show on which conditions future studies should be focused and form a necessary first step in identifying subgroups of diseases benefiting from probiotic treatment.

In conclusion, in the current study, it is suggested that SLAB51™ can have a role in the treatment of GI conditions in dogs. In a subset of patients with CE, these probiotics can be used alone, as suggested by the presence of a low number of dogs identified with likely PRE. However, in most dogs in this retrospective study, these probiotics were combined with other treatments and diets, making a clear-cut analysis of the probiotic effect more challenging. These responses suggest that SLAB51™ can be part of a multimodal approach to chronic enteropathies in situations where other therapies failed to fully control clinical signs. Prospective studies using this probiotic blend are indicated to fully assess their effect on treating CE in dogs.

## REFERENCES

- Arslan H., Aksu D., Terzi Gülel G., Nisbet C. (2012). Therapeutic effects of probiotic bacteria in parvoviral enteritis in dogs. *Revue de Médecine Veterinaire* 163, 55-59.
- Blaabjerg S., Artzi D.M., Aabenhus R. (2017). Probiotics for the Prevention of Antibiotic-Associated Diarrhea in Outpatients - A systematic review and meta-analysis. *Antibiotics* 6(4), 21.
- Castagliuolo I., Riegler M.F., Valenick L., LaMont J.T. & Pothoulakis C. (1999). *Saccharomyces boulardii* protease inhibits the effects of *Clostridium difficile* toxins A and B in human colonic mucosa. *Infection and Immunity* 67, 302-307.
- Collado M.C., Grzeskowiak Ł., Salminen S. (2007). Probiotic strains and their combination inhibit in vitro adhesion of pathogens to pig intestinal mucosa. *Current Microbiology* 55, 260-265.
- di Vito R., Conte C., Traina G. (2022). A multi-strain probiotic formulation improves intestinal barrier function by the modulation of tight and adherent junction proteins. *Cells* 11(16), 2617.
- Dandrieux J.R. (2016). Inflammatory bowel disease versus chronic enteropathy in dogs: are they one and the same? *Journal of Small Animal Practice* 57(11), 589-599.
- Dandrieux J.R.S., Mansfield C.S. (2019). Chronic enteropathy in canines: prevalence, impact and management Strategies. *Veterinary Medicine Auckland, N.Z.* 10, 203-214.
- FAO/WHO. Evaluation of health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. *Report on Joint FAO/WHO Expert Consultation 2001.*
- Huang R, Xing H.Y, Liu H.J., Chen Z.F., Tang B.B.(2021). Efficacy of probiotics in the treatment of acute diarrhea in children: a systematic review and meta-analysis of clinical trials. *Translational Pediatrics* 10(12), 3248-3260.
- Hill C., Guarner F., Reid G., et al.(2014). The International



- Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *National Reviews Gastroenterology and Hepatology* 11, 506-514.
- Jensen A.P., Bjørnvad C.R. (2019). Clinical effect of probiotics in prevention or treatment of gastrointestinal disease in dogs: A systematic review. *Journal of Veterinary Internal Medicine* 33(5), 1849-1864.
- Jergens A.E., Heilmann R.M. (2022) Canine chronic enteropathy - Current state-of-the-art and emerging concepts. *Frontiers in Veterinary Science* 9, 923013.
- Jones S.E., Versalovic J. (2009). Probiotic *Lactobacillus reuteri* biofilms produce antimicrobial and anti-inflammatory factors. *BMC Microbiology* 9, 35.
- Kathrani A, Werling D, Allenspach K. (2011). Canine breeds at high risk of developing inflammatory bowel disease in the south-eastern UK. *Veterinary Record* 169(24), 635.
- Kelley R.L., Minikhiem D., Kiely B., O'Mahony L., O'Sullivan D., Boileau T., Park J.S. (2009). Clinical benefits of probiotic canine-derived *Bifidobacterium animalis* strain AHC7 in dogs with acute idiopathic diarrhea. *Veterinary Therapeutics: Research in Applied Veterinary Medicine*, 10(3), 121-130.
- Lee Y.K., Puong K.Y., Ouwehand A.C., Salminen S. (2003). Displacement of bacterial pathogens from mucus and Caco-2 cell surface by lactobacilli. *Journal of Medical Microbiology* 5, 925-930.
- Marchesi M.C., Timpano C.C., Busechian S., Pieramati C., Rueca F. (2017). The role of diet in managing inflammatory bowel disease affected dogs: a retrospective cohort study on 76 cases. *Veterinaria Italiana* 53(4), 297-302.
- Medellin-Pena M.J., Wang H., Johnson R., Anand S., Griffiths M.W. (2007). Probiotics affect virulence related gene expression in *Escherichia coli* O157:H7. *Applied and Environmental Microbiology* 73, 4259-4267.
- Nixon S.L., Rose L., Muller A.T. (2019). Efficacy of an orally administered anti-diarrheal probiotic paste (Pro-Kolin Advanced) in dogs with acute diarrhea: A randomized, placebo-controlled, double-blinded clinical study. *Journal of Veterinary Internal Medicine* 33: 1286-1294.
- Pagnini C., Saeed R., Bamias G., Arseneau K.O., Pizarro T.T., Cominelli F. (2010). Probiotics promote gut health through stimulation of epithelial innate immunity. In: *Proceedings of the National Academy of Science USA*, 107(1), 454.
- Ramezani Ahmadi A., Sadeghian M., Alipour M., Ahmadi Taheri S., Rahmani S., Abbasnezhad A. (2020). The effects of probiotic/synbiotic on serum level of zonulin as a biomarker of intestinal permeability: a systematic review and meta-analysis. *Iranian Journal of Public Health* 49(7), 1222-1231.
- Rossi G., Pengo G., Caldin M., Palumbo Piccionello A., Steiner J.M., Cohen N.D., Jergens A.E., Suchodolski J.S. (2014). Comparison of microbiological, histological, and immunomodulatory parameters in response to treatment with either combination therapy with prednisone and metronidazole or probiotic VSL#3 strains in dogs with idiopathic inflammatory bowel disease. *PLoS One* 10, 9(4) - e94699.
- Rossi, G., Jergens, A., Cerquetella, M., Berardi, S., Di Cicco, E., Bassotti, G., Pengo, G., Suchodolski, J. S. (2018). Effects of a probiotic (SLAB51™) on clinical and histologic variables and microbiota of cats with chronic constipation/megacolon: a pilot study. *Beneficial Microbes* 9(1), 101-110.
- Rossi G., Gioacchini G., Pengo G., Suchodolski J. S., Jergens A.E., Allenspach K., Gavazza, A. Scarpona S., Berardi S., Galosi L., Bassotti G., Cerquetella M. (2020). Enterocolic increase of cannabinoid receptor type 1 and type 2 and clinical improvement after probiotic administration in dogs with chronic signs of colonic dysmotility without mucosal inflammatory changes. *Neurogastroenterology and Motility* 32(1), e13717.
- Scahill K., Jessen L.R., Prior C., Singleton D., Foroutan F., Ferran A.A., Arenas C., Bjørnvad C.R., Lavy E., Allerton F., Weese J.S., Allenspach K., Guardabassi L., Unterer S., Bodnárová T., Windahl U., Brennan M.L., Werner M. (2024). Efficacy of antimicrobial and nutraceutical treatment for canine acute diarrhoea: A systematic review and meta-analysis for European Network for Optimization of Antimicrobial Therapy (ENOVAT) guidelines. *The Veterinary Journal*, volume 303, Article 106054
- Schmitz S., Henrich M., Neiger R., Werling D., Allenspach K. (2013). Comparison of TNF $\alpha$  responses induced by Toll-like receptor ligands and probiotic *Enterococcus faecium* in whole blood and peripheral blood mononuclear cells of healthy dogs. *Veterinary Immunology and Immunopathology* 153, 170-174.
- Schmitz S., Henrich M., Neiger R., Werling D., Allenspach K. (2014). Stimulation of duodenal biopsies and whole blood from dogs with food-responsive chronic enteropathy and healthy dogs with toll-like receptor ligands and probiotic *Enterococcus faecium*. *Scandinavian Journal of Immunology* 80, 85-94.
- Stavroulaki E.M., Suchodolski J.S., Xenoulis P.G. (2023). Effects of antimicrobials on the gastrointestinal microbiota of dogs and cats. *The Veterinary Journal* 291, 10592.
- Strompfová V., Marciňáková M., Pogány Simonová M., Laukova A., Fialkovičová M. (2008). Probiotic strain *Lactobacillus fermentum* CCM 7421, canine isolate applied to dogs suffering from gastrointestinal disorders. *International Journal of Probiotics and Prebiotics* 2, 233-238.
- Vakadaris G., Stefanis C., Giorgi E., Brouvalis M., Voidarou C., Kourkoutas Y., Tsigalou C., Bezirtzoglou E. (2023). The role of probiotics in inducing and maintaining remission in crohn's disease and ulcerative colitis: a systematic review of the literature. *Biomedicines* 11(2):494.
- Ziese A.L., Suchodolski J.S., Hartmann K., Busch K., Anderson A., Sarwar F., Sindern N., Unterer S. (2023). Effect of probiotic treatment on the clinical course, intestinal microbiome, and toxigenic *Clostridium perfringens* in dogs with acute hemorrhagic diarrhea. *PLoS One* 13(9) - e0204691. Erratum in: *PLoS One* 18(1) - 2023 - e0280539.

