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Biotics in the management of gastrointestinal disorders in dogs and cats

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Summary

The gut microbiome is integral to gastrointestinal health in dogs and cats, with imbalances (dysbiosis) linked to conditions like diarrhoea and chronic enteropathy. Pre-, pro-, and postbiotics (biotics) are emerging as therapeutic options for managing these disorders, especially due to their potential antibiotic-sparing effects.

Prebiotics, often traditional soluble and insoluble dietary fibre from plants (e.g. beet pulp, psyllium), or smaller extracts and derivatives like glucans or oligosaccharides, have been shown to have some benefits, likely through serving as nutrition for the commensal microbiota, but clinical effects - for example on large bowel diarrhoea - are often minor. Plant polyphenols are of increasing interest for their potentially strong anti-inflammatory actions, and small pilot trials in dogs with colitis seem promising.

The evidence-based use of probiotics is hampered by the lack of direct comparisons between different bacterial strains or synbiotics (combining pre- and probiotics) for dogs, and the general paucity of prospective studies in cats. For acute uncomplicated diarrhoea, single-strain probiotics like *Enterococcus faecium*, have resulted in some clinical improvement in dogs, but a recent European consensus concluded that the evidence is not strong enough to advocate for or against probiotic use in acute diarrhoea. Specific lactic acid bacteria blends have shown clinical benefits compared to supportive treatment alone in conditions like canine Acute Haemorrhagic Diarrhoea Syndrome, and parvoviral enteritis. In cats, *E. faecium* might reduce relapses of tritrichomoniasis. Similar probiotic blends might be a useful adjunctive treatment for chronic gastrointestinal conditions like canine chronic enteropathy or feline constipation. One study reports an improvement of clinical signs and serum albumin in dogs with protein-losing enteropathy given live *Saccharomyces boulardii*. Unfortunately, from available studies there is no evidence that co-administration of pro- or synbiotics will prevent or alleviate antibiotic-induced diarrhoea and dysbiosis in dogs or cats.

Postbiotics, which are preparations containing inactivated microbial cells or cell components, with or without their metabolites, are of potential interest to achieve similar effects to probiotics but without relying on live microorganisms. They remain so far unexplored as treatment for gastrointestinal conditions in small animals.

While biotics seem to be generally safe in companion animals, the overall evidence for their use is limited. However, biotic approaches provide promising additional tools for managing GI health in dogs and cats. More evidence in the form of comparative trials in well-define conditions are needed to explore their full potential and support their more wide-spread evidence-based integration into small animal veterinary practice.

1. Introduction to Biotics

The gut microbiome plays a vital role in the overall health of dogs and cats, particularly in gastrointestinal (GI) health. Imbalances in gut microbiota, termed dysbiosis, are associated with a range of GI disorders, such as acute or chronic diarrhoea, including chronic enteropathy (CE). Emerging evidence tentatively supports the therapeutic use of pre-, pro- or synbiotics (collectively:

biotics) to restore gut homeostasis and manage these conditions. This article explores their evidence-based use in the treatment of GI disorders in dogs and cats.

2. Prebiotics Mechanism of Action

Prebiotics are non-digestible food components, usually dietary fibres, that selectively stimulate the growth of beneficial gut bacteria. These include for example fructooligosaccharides (FOS), mannanoligosaccharides (MOS), but also resistant starches (RS), beta-glucans and inulin, some of which can promote the proliferation of beneficial bacterial and their metabolites, such as short chain fatty acids (SCFAs), within the intestine.

2.1. Prebiotics in Dogs with GI Disorders

Even though dietary fibres have been used traditionally to maintain faecal quality, provide laxation, reduce faecal odour, and modulate fermentative end-products (see postbiotics below) in dogs, their sole use in specific canine GI conditions is not well documented.

One relatively recent study assessed a commercial high fibre diet (a mixture of soluble and insoluble fibres largely derived from beet pulp) compared to a diet with a more standard fibre content in shelter dogs with acute colitis (1). Faecal scores improved in all dogs on the high fibre diet, while this was only achieved in around 55% of the dogs on the standard diet. However, a small number of dogs that continued to show diarrhoea were found to harbour intestinal parasites like *Giardia* sp. and Cryptosporidium, which could have skewed results. The absence of assessments of any gut health related parameters beyond faecal scoring (e.g. no microbiome or metabolome analysis) and the absence of a confirmed diagnosis are additional limitation of this study.

Clinical benefits of increased fibre intake have been reported for a long time in a subpopulation of dogs with chronic idiopathic large bowel diarrhoea, leading to the term 'fibre-responsive colitis'. This syndrome is closely related to and overlaps with lymphoplasmacytic colitis (a form of CE) and irritable bowel syndrome (IBS) (2). However, primary literature on this subject is scarce, and can be nearly exclusively traced back to a single retrospective study using psyllium hydrophilic mucilloid (from seeds or husk of the plant *Plantago ovata*, consisting of approximately 90% soluble fibre) in dogs with chronic colitis that had failed previous (mostly dietary) treatment attempts (3). The response of 27 dogs with follow-up from this study was considered excellent in 63%, very good in 22% and good in 11%, but it is unclear how this owner-reported information was collected or quantified (3).

For dogs with CE, 3 studies have investigated similar blends of neutraceuticals, namely a combination of the glucosaminoglycan (GAG) chondroitin sulphate, and the prebiotics alpha-glucan butyrogenic RS, beta-glucans and MOS in 2 studies (4,5); and a separate assessment of beta-glucan with and without MOS in another study (6). One of the former studies assessed faecal metabolites in response to the supplementation; and found that the change to a hydrolyzed diet alone (done in all dogs) significantly increased metabolites that protect gut cell membrane integrity, with a possible additional beneficial effect on lipid metabolism in dogs treated with the GAG and the prebiotic blend (5). Serum markers indicative of intestinal permeability and antioxidant capacity also improved in this and another study with this supplement, while no significant difference was found between groups for clinical activity scores, histological inflammation score or faecal microbiota composition (4,5). Similarly, beta-glucan alone or in addition to MOS did not have a superior effect on clinical severity, faecal scores, blood parameters, faecal lactic acid, or short- and branched-chain fatty acids compared to placebo in another study, but had variable effects on the microbiota composition: an increase in Firmicutes and Bacteroidetes, which could be interpreted as beneficial (as bacteria in these phyla are

generally considered SCFA producers), but also an increase in Proteobacteria (in the beta-glucan treatment group only) (6). This latter phylum contains the family of Enterobacteriaceae, increases of which are a common hallmark of dysbiosis in CE (7).

There is also recent increasing interest in the use of specific plant compounds called polyphenols (including flavonoids, tannins and phenolic acids and their derivatives) as prebiotics. A potential role in managing acute diarrhoea in dogs has been suggested (8), and one study has used a polyphenol-enriched diet as treatment in dogs with chronic colitis (9). Overall, there was an improvement or resolution of colitis signs in 22/31 (71%) of dogs within 2 days, and by the end of the study (day 56) all dogs had either improved or resolved clinical signs (9).

2.2. Prebiotics in Cats with GI Disorders

Research into prebiotic use in cats is more limited compared to dogs, with the available evidence only derived from feeding studies in healthy cats. For example, one study reported that short-term supplementation with FOS, galactooligosaccharides (GOS) or their combination led to improved faecal microbiota composition (increase in *Bifidobacterium* spp. populations), reduced faecal pH, increased faecal SCFAs like butyrate, valerate and acetate, while faecal protein catabolites, peripheral blood parameters and faecal dry matter concentration and output did not change (10).

The use of prebiotics in cats with acute GI disease or Inflammatory Bowel Disease (IBD) has not been explored, hence further studies are needed to determine the specific benefits.

3. Probiotics: Mechanism of Action

According to the World Health Organisation, probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. This can be achieved through local effects by improving or restoring the gut flora, or distant effects in other body systems and organs. Probiotic strains are thought to help restore microbial balance by inhibiting pathogenic bacteria in the intestine, enhancing mucosal tolerogenic immunity, producing antimicrobial substances, and reinforcing the intestinal barrier function and integrity (11).

3.1. Synbiotics: Combining Prebiotics and Probiotics

Synbiotics, which combine prebiotics and probiotics, offer potential synergistic benefits for the treatment of GI disorders. By providing both a substrate for beneficial bacteria (prebiotics) and live beneficial microorganisms (probiotics), synbiotics are thought to enhance the colonization and activity of probiotics in the gut. As most products marketed for dogs and cats in the UK are synbiotics with vastly different prebiotic ingredients, and clinical trials have less commonly used pure probiotics compared to commercially available synbiotics, the evidence-based use of pro- and synbiotics will be discussed together below (see also table 1 for a summary). A lot of other allegedly beneficial ingredients of synbiotics, like proprietary prebiotic blends or “natural” extracts from a variety of plants (e.g. chicory, pumpkin, blueberries, curcuma) are difficult to scrutinise scientifically and hence to compare, as their sources are unclear and no studies proving their health benefits exist.

Table 1. Summary of evidence for the use of specific probiotics in GI disorders of dogs and cats.
AHDS = acute haemorrhagic diarrhoea syndrome; ARE = antibiotic-responsive chronic enteropathy; FRE = food-responsive chronic enteropathy; n/a = no information available, PLE = protein-losing enteropathy.

Probiotic strain (alone or as part of a synbiotic)	**Has shown some benefit in…**	**No benefit in…**
Enterococcus faecium (SF68 or NCIMB 14015)	Dogs: Acute uncomplicated "idiopathic" diarrhoea/ shelter- or kennelling stress- associated diarrhoea	Dogs: Chronic enteropathy/ Inflammatory Bowel Disease Giardiasis Ancylostoma infection
	Cats: *Tritrichomonas blagburnii* infection recurrence	Cats: Kennelling-stress -associated diarrhoea
Bifidobacterium animalis AHC7	Dogs: Acute uncomplicated "idiopathic" diarrhoea	n/a
Bacillus licheniformis-fermented products (BLFP)	Cats: Improvement of chronic diarrhoea and associated beneficial microbiota changes	Dogs: No studies
Bacillus subtilis	Dogs (healthy dogs only): Improves faecal parameters like protein digestibility, pH, Short Chain Fatty Acids, ammonia levels	Dogs & cats: No studies in any GI health condition
Lactic acid bacteria mixture (*L. acidophilus* NCC2628, *L. acidophilus* NCC2766, *L. johnsonii* NCC2767)	n/a	Dogs: In FRE: no clinical benefit or effect on duodenal and colonic cytokine expression
Lactic acid bacteria mixture (ProViable D-C, see table 2)	Cats: chronic diarrhoea/ enteropathy	Dogs: No studies
Lactobacillus rhamnosus	n/a	Dogs: ARE
Lactic acid bacteria mixture 'De Simone Formulation' (see table 2)	Dogs: Chronic enteropathy AHDS Parvovirosis	Cats: No studies
Lactic acid bacteria mixture SLAB51 (see table 2)	Dogs: Chronic enteropathy	n/a
	Cats: Constipation/ megacolon	n/a
Saccharomyces boulardii	Dogs: Chronic enteropathy PLE	Cats: No studies

3.2. Pro- and Synbiotics in Dogs with GI Disorders

Probiotic strains commonly marketed for companion animals in the UK include *Enterococcus faecium* (EF), *Bacillus subtilis*, different *Lactobacilli*, *Bifidobacterium*, or a combination of them. Unfortunately, a lot of the available strains, especially *Bacillus* sp. and *Lactobacilli*, have little associated evidence to support their use in canine GI conditions. Live yeasts like *Saccharomyces boulardii* are less frequently available, although yeast extracts often provide prebiotics like MOS in synbiotic preparations.

Pro- and synbiotics have been studied in dogs with acute GI disorders of different causes, and recently summarised in a systematic review (12), including 12 studies. No meta-analysis could be performed due to the significant heterogeneity of studies and the evidence was not sufficiently robust to determine the effectiveness and clinical relevance of probiotics. Re-analysis including 2 more recent studies for the European Network for Optimization of Antimicrobial Therapy (ENOVAT) guidelines, that equally concluded that the evidence is of substandard quality to make either recommendations for or against the use of probiotics in acute diarrhoea (13,14).

Examples of primary studies include the administration of *Bifidobacterium animals* AHC7 (15) in acute uncomplicated idiopathic diarrhoea, for example in a shelter environment (16,17). Here, neutraceutical administration was not inferior to other potentially more harmful or controversial treatments like antibiotics (15,17) and small beneficial effects on the duration of diarrhoea were observed (15,16). In dogs with parasitic infections like Giardiasis (18) or Ancylostoma infection (19), no lasting effect of probiotic EF was seen.

In Acute Haemorrhagic Diarrhoea Syndrome (AHDS), a disease likely associated with an acute 'overgrowth' of NetF toxin-producing *Clostridium perfringens* (20), a probiotic blend containing a high concentration of 9 different bacterial strains often designated the 'De Simone Formulation' (DSF, see table 2) decreased clinical severity, reduced *C. perfringens* abundance and associated enterotoxins, and improved faecal microbiota composition (21). The same probiotic mixture given to dogs with parvoviral enteritis achieved significant clinical improvement, higher white blood cell counts, and a reduction in mortality rate in comparison to standard of care treatment alone (22).

In chronic GI conditions, such as canine CE, some probiotics with initial anti-inflammatory *effects in vitro*, failed to elicit similar effects *in vivo*, including EF (23,24) and a cocktail of Lactobacilli (25,26). *Lactobacillus rhamnosus* GG failed to prolong the asymptomatic period in tylosin-responsive CE (27). Probiotic blends like DSF, which is also used in people with IBD, seem to be the most promising probiotics for CE in dogs: In one study, DSF was clinically as effective in dogs with otherwise non-responsive CE than a combination treatment consisting of metronidazole and prednisolone (28). In addition to the clinical efficacy, this study demonstrated an increase in mucosal regulatory T-cell markers only of the DSF treated dogs, leading to a more tolerogenic microenvironment in the GI tract. In another study, it was shown that the DSF probiotic also enhanced the expression of tight junction proteins in the mucosa of dogs with CE (29). There is also emerging evidence that a similar probiotic mixture called SLAB51^{TM} (see table 2), can lead to clinical improvement in dogs with CE (author's observations, article in press).

A study in dogs with Protein-losing enteropathy (PLE) showed a significant improvement in clinical signs using *S. boulardii* as adjunctive treatment (30). While this study was small, 3 dogs given *S. boulardii* also showed a significant improvement of serum albumin values compared to 3 dogs with PLE not given this probiotic. These preliminary data have not been confirmed by a larger study.

Table 2. Probiotic strains found in 3 probiotic blends used in small animals. *Trade name Vivomixx® (Ormendes SA, Switzerland) in the UK. $Trade name Sivomixx® (Ormendes SA, Switzerland), † Nutramax Laboratories, UK

'De Simone Formulation' (DSF)*	**SLAB51$**	**Proviable-DC or Forte†**
• *Lactobacillus paracasei* NCIMB 30439 • *Lactobacillus plantarum* NCIMB 30437 • *Lactobacillus acidophilus* NCIMB 30442 • *Lactobacillus delbrueckii* subspecies *bulgaricus* NCIMB 30440 (reclassified as *L. helveticus*) • *Bifidobacerium longum* NCIMB 30435 (*reclassified as B. lactis*) • *Bifidobacterium breve* NCIMB 3041 • *Bifidobacterium infantis* NCIMB 30436 (reclassified as *B. lactis*) • *Streptococcus salivarus* subspecies *thermophilus* NCIMB 30438	• *Streptococcus thermophilus* DSM32245 • *Lactobacillus acidophilus* DSM32241 • *Lactobacillus plantarum* DSM32244 • *Lactobacillus casei* DSM32243 • *Lactobacillus helveticus* DSM32242 • *Lactobacillus brevis* DSM27961 • *Bifidobacterium lactis* DSM32246 • *Bifidobacterium lactis* DSM32247	• *Enterococcus faecium* NCIMB 30183 • *Streptococcus salivarus* subspecies *thermophilus* NCIMB 30189 • *Lactobacillus acidophilus* NCIMB 30184 • *Lactobacillus delbrueckii* subspecies *bulgaricus* NCIMB 30186 • *Lactobacillus casei* subspecies *rhamnosus* NCIMB 30188 • *Bifidobacterium bifidum* NCIMB 30179 • *Lactobacillus plantarum* NCIMB 30187

3.3. Pro- and Synbiotics in Cats with GI Disorders

Only one study has assessed the effect of probiotics on acute diarrhoea in cats, and no effect on the prevalence or duration of shelter-associated diarrhoea was found (16) (see table 1). Evidence for the adjunctive use of an EF-containing synbiotic in feline *Tritrichomonas blagburnii* (formerly *T. foetus*) infection is based on a small clinical trial, where it did not accelerate time to clinical improvement compared with ronidazole alone, but significantly reduced relapses (31).

There are 2 studies involving the administration of biotics in cats with chronic diarrhoea. In one of these, the cats were well phenotyped and most likely suffered from IBD, as extra-gastrointestinal and infectious causes of diarrhoea led to inclusion from the study (32). However, GI histopathology was not performed, so the type and severity of mucosal pathology was not known. In this trial, 53 cats with variable duration of diarrhoea (3 weeks to > 6 months) completed the supplementation period of 21 days with ProViable DC® (see table 2). Of those, 38 (72%) improved with probiotic supplementation, while 13 had no change and 2 worsened. However, a large proportion of cats in all categories received additional medications, and the cats' diet was not standardised. In the other study, a different probiotic called *Bacillus licheniformis*-fermented products (BLFP) was given to a small group of cats with otherwise ill-defined chronic diarrhoea (33). BLFP is obtained from solid-state fermentation and contains *Bacillus* spores (stable in the environment) as well as secondary metabolites, such as biosurfactants (33). Diarrhoea improved or resolved in 6/8 cats and presumed beneficial changes of the microbiota composition were also seen.

Another study found that the SLAB51™ blend might be beneficial in feline chronic constipation or idiopathic megacolon, based on findings from a small pilot study with 10 cats, where all cats were reported to improve clinically (34).

3.4. Biotics in Antibiotic-Associated Dysbiosis and Diarrhoea

One of the major potential clinical applications of probiotics could be in preventing and managing antibiotic-associated gastrointestinal signs (AAGS) in companion animals. As antibiotics disrupt the gut microbiota, leading to diarrhoea and dysbiosis (35), probiotics could promote faster recovery by restoring beneficial bacterial populations.

However, evidence of a significant prophylactic or metaphylactic effect of giving biotics with antibiotics to prevent or alleviate signs of AAGS or dysbiosis is lacking for both dogs (36) and cats (37,38) (see table 3). More studies on microbiota modifying therapies are needed before any can be recommended to treat or prevent AAGS in dogs and cats.

Table 3. Summary of study results in healthy dogs and cats with induced antibiotic-associated gastrointestinal signs (AAGS). EF = *Enterococcus faecium.*

	Antibiotic	**Biotic**	**Effect**
Dogs	Enrofloxacin + Metronidazole	Proviable-Forte (see table 2) + *Saccharomyces boulardii* + beta-glucan*	No beneficial effect on frequency of vomiting, hyporexia and diarrhoea, but mildly better food intake compared to placebo
Cats	Clindamycin	Proviable DC (see table 2) + FOS and arabinogalactan	50% of cats in biotic group had to be withdrawn due to AAGS severity. Antibiotic-induced microbiota dysbiosis not alleviated by the administration of biotic compared to placebo.
	Amoxicillin-clavulanate	EF SF68	No beneficial effect on frequency of vomiting or occurrence of diarrhoea. Potential small effect on reducing severity of diarrhoea (e.g. better faecal scores) in EF treated cats compared to placebo. No alleviating effect on microbiota dysbiosis.

4. Postbiotics

Research indicates that the major health-promoting effect of gut microbiota may be attributable to their non-viable byproducts, so called postbiotics (39). In 2021, a standardised definition for postbiotics was proposed by the International Scientific Association of Probiotics and Prebiotics (ISAPP) as 'preparations of inanimate microorganisms and/ or their components that confer a health benefit on the host'. This clarifies that postbiotics must contain inactivated microbial cells or cell components, with or without metabolites, not the metabolites alone (40). Cellular components might be peptidoglycans, lipopolysaccharide and extracellular vesicles, and cellular metabolites include bacteriocins, SCFAs, biotin, enzymes and organic acids (see figure 1). These components are typically released by live probiotics through fermentation processes or via lysis. Potential health benefits of postbiotics, especially in the context of chronic intestinal inflammation, have been reviewed elsewhere (39), but are very similar to the benefits of live probiotics and include inhibition of pathogen growth, and immunomodulation (39). However, as of yet, no prospective studies using postbiotics as a therapeutic intervention in any GI condition in companion animals are available.

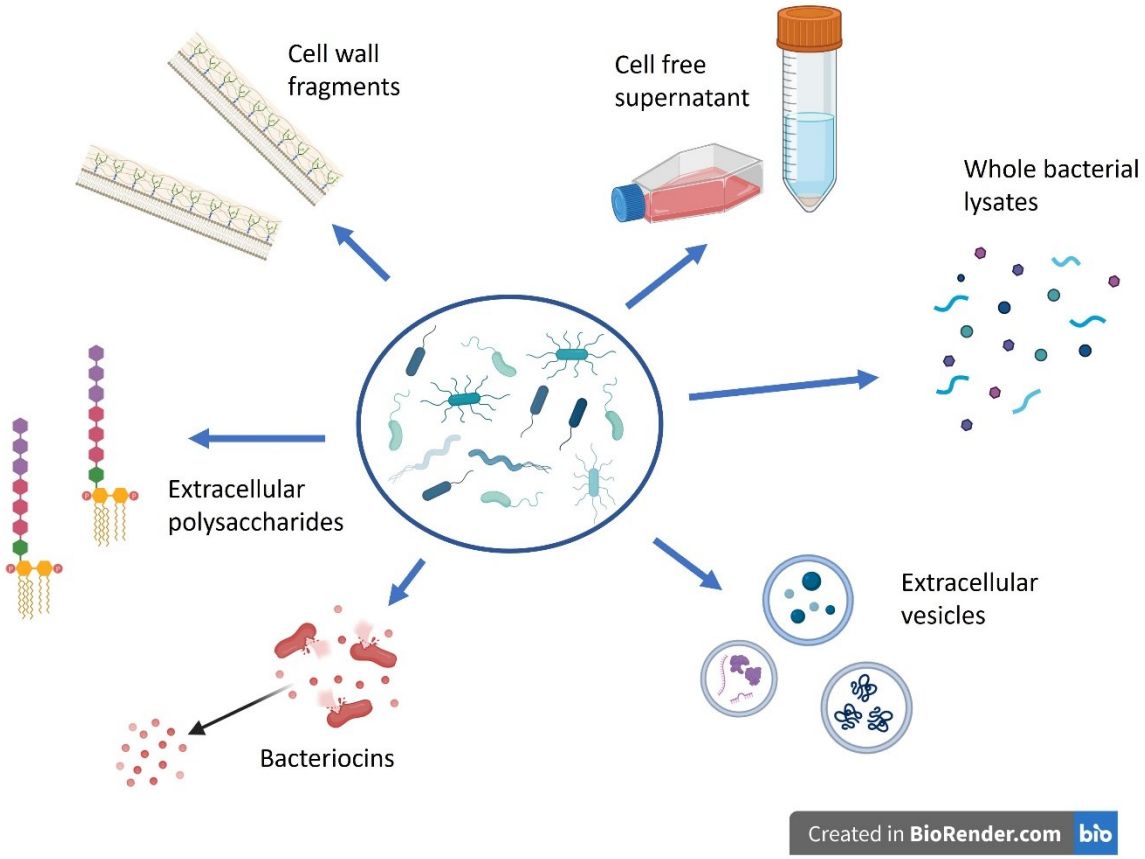

Figure 1. Different types of postbiotics derived from probiotics.

5. Discussion of Challenges and Considerations for the Use of Biotics

Despite the growing body of evidence tentatively supporting the use of biotics in treating GI disorders in dogs and cats, particularly in chronic enteropathy/ chronic colitis/ constipation, several challenges remain. The evidence is limited and inconsistent, with study results variable and not easy to compare due to differences in study design, animal populations, and the specific probiotic strains or synbiotic formulations used. This is particularly evident for cases of acute diarrhoea. The potential variability in individual responses to these supplements is another such challenge, as animals with different baseline microbiota compositions may respond differently to supplementation.

Additionally, the strain specificity of probiotics is critical, as not all strains exert the same effects, even within the same species (41). This remains largely unexplored in dogs and cats and makes it difficult to generalize the benefits of even very similar pro- or synbiotic products to larger populations.

Another important consideration is the quality of available probiotic products, mainly the survival and stability of probiotics during storage and GI transit (11). Probiotic formulations must ensure that live microorganisms can reach the intestines in adequate numbers to exert their effects. Pre-, pro- and synbiotic products are not regulated like drugs, as they are often sold over-the-counter as nutritional supplements. As they do not fall under the same governance and regulations as drugs, both from the manufacturing and labelling point of view, this hinders transparent assessment of the source and quality of ingredients as well increases concerns about the validity of any associated health claims.

Adverse effects of probiotics are not well documented in companion animals. Potentially, effects like bloating or worsening diarrhoea can occur in some animals, likely due to direct changes in ingesta fermentation or their indirect consequences (for example changes in GI motility). The vast majority of human clinical trials with probiotics do not give rise to major safety concerns. However, a few serious adverse effects have been documented in people, like sepsis or fungaemia from the probiotic in immunocompromised hosts. At the moment, no specific contraindications for the use of live probiotics have been identified in dogs and cats (11).

6. Conclusion

While biotics seem to be generally safe in companion animals, evidence for their use is limited to a number of small studies that are not easy to compare. There is likely to be an increasing body of evidence for the use of specific prebiotics in the future, either as supplements, or already incorporated in specific foods. For pro- and synbiotics, careful consideration must be given to the choice of strain, dose, individual animal factors and disease indication to optimize outcomes. There is a considerable knowledge gap remaining regarding the most appropriate use of biotics in acute diarrhoea; and in chronic GI disease, biotics are unlikely to emerge as a stand-alone treatment.

Nonetheless, biotics should be considered potentially beneficial adjunctive treatments in dogs and cats with both acute and chronic GI signs. In canine CE it seems reasonable to deduct that specific probiotic cocktails can address one of the multifactorial aspects of disease pathogenesis, which is why clinical responses will remain variable between individuals.

An indirect benefit of the use of biotics is the reduction of the administration of antibiotics, which has both individual and hence less devastation of their individual microbiota. Based on the limited evidence available, co-administration of biotics alongside antibiotics is unlikely to prevent or restore

AAGS and associated dysbiosis, while any health-promoting effect of potential postbiotics remains unexplored in small animals.

As research continues to expand, and more evidence for specific probiotic strains used for defined conditions emerges, these supplements may – potentially together with other microbiota-modifying treatment approaches – play an increasingly important role in the management of GI disorders in dogs and cats.

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