

PROBIOTICS: HEALTHY FROM THE INSIDE OUT

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“Natural forces within us are the true healers of disease.” Hippocrates

Introduction

A pet's wellness (as is the case for people too) relies on a functioning gastrointestinal tract for many reasons, including the presence therein of approximately seventy percent of the immune system and more neurons than anywhere else in the body except the brain! It is estimated that there are many times the number of bacteria (representing more than 500 species) in the gastrointestinal tract than there are cells in the body (and those number in the trillions). In health there is a balance in the intestines between beneficial bacteria and harmful bacteria. The beneficial (“good”) bacteria contribute directly to the maintenance or restoration of health through multiple mechanisms, including the stimulation of the immune system, the processing of nutrients, and the production of vitamins and fatty acids that support normal intestinal function.

The acknowledgements of the importance of gastrointestinal microbes as well as the concept of managing both wellness and illness “from the inside out” to encourage the growth and presence of “good” bacteria (while discouraging the growth and presence of “bad” bacteria) have been around for well over a hundred years. In the middle to late 1800's, Louis Pasteur, Joseph Lister and Robert Koch advanced the theory (now a cornerstone of modern medicine) that microorganisms are the cause of many diseases. The Russian scientist Metchnikoff, in the early 1900's, recognized that some gut bacteria could help *protect* mammals from infection. There has been a resurgence of interest lately in this area of microbiology (some even call it a revolution!) given that technology now exists to create viable and stable products containing beneficial microbes, i.e. “probiotics” (from the Greek “for life”).

It is important to first answer a few questions, reviewing terminology (before detailing mechanisms of action, indications, precautions and evaluation guidelines) to ensure proper understanding of this topic, especially given that misinformation is common.

What are microbes?

Microbes, also known as microorganisms, are very tiny life forms, best visualized under a microscope. Microbes refer not only to bacteria, but also yeast and protozoa as well as some other organisms too small to be seen with the naked eye. “Microbiota”, a term interchangeable with “microflora”, refers to the microbes that inhabit a certain area. In the context of this discussion, that area will most often be the digestive tract.

What are probiotics?

Probiotics are beneficial *live* microbes that when ingested help to support the pet's intestinal and overall health. Most commercially available probiotics contain certain strains of *Lactobacillus* species, *Bifidobacterium* species and/or *Enterococcus* species.

What are prebiotics?

Prebiotics are most commonly complex carbohydrates that can be used as a food source by the probiotics, especially within the large intestine.¹ Prebiotics therefore support the growth of the probiotics within the intestinal tract and help them compete against harmful bacteria for colonization of the intestines. Examples of prebiotics are fructooligosaccharides (FOS), mannanoligosaccharides (MOS), arabinogalactans, and inulin.

Combinations of probiotics and prebiotics (combinations referred to as “synbiotics”) are often found in commercial products², based on the understanding that the prebiotics will help the probiotics survive, colonize the intestinal tract, and produce a beneficial effect. A study in dogs³ confirmed a benefit to administering a probiotic strain in conjunction with FOS over administration of the probiotic alone.

What are Colony Forming Units (CFUs)?

Colony Forming Units (CFUs) refer to the number of microbes, either bacteria or yeast, that is capable of dividing and forming colonies. The term CFUs (often found on probiotic product labels, marketing, and literature) represents a way of tabulating “live and healthy microbes”.

Mechanisms of action of probiotics

The mechanisms of action of probiotics are not completely understood but are variable and complex.

Probiotics compete with potentially harmful microbes in the digestive tract for adhesion to the intestinal mucosa, thereby interfering with the establishment of the harmful microbes. This should not be interpreted to mean that probiotics eliminate all potentially harmful microbes but rather lower their population to limit their damaging effects. The competitive exclusion by probiotics of harmful intestinal microbes, along with the promotion of an environment not conducive to pathogen growth, is also a beneficial effect against diarrhea caused by infectious and parasitic agents, including, but not limited to, rotaviruses, *Escherichia coli*, *Salmonella* species, *Coccidia* species, common roundworms, hookworms, *Cryptosporidium* and *Giardia* species.⁴

Probiotics help the immune system function properly. The immune system, when confronted with potential threats, may respond and contain damage from harmful microbes or may overreact and actually cause problems (for example, an unrestrained immune system may act against harmless substances - such as dust or pollen - resulting in autoimmune disorders and allergic responses). Probiotics enhance the immune system’s appropriate defenses and responses.

The establishment and maintenance of healthy intestinal function and microbionics in young and adult dogs and cats is facilitated by probiotics through their manufacture of certain B vitamins (including niacin (B3), pyridoxine (B6), folic acid and biotin) and fatty acids, the improved efficiency of the digestive tract (probiotics aid in the breakdown of food particles by stimulating digestive enzymes) and the killing or deactivating of hostile

disease-causing bacteria (by changing the local levels of acidity, by depriving pathogenic bacteria of their nutrients, or by producing antibacterial substances).⁵

Scientific studies and efficacy of probiotics

Regarding efficacy, numerous and solid scientific studies have demonstrated the benefits of probiotics in people for a variety of disorders (including antibiotic-associated diarrhea, colitis, traveler's dysentery, acute diarrhea, and prevention and treatment of urinary and vaginal infections). One study in young dogs showed that a dietary probiotic (*Enterococcus faecium*) enhanced specific immune function, including the immune capacity of newly weaned pups.⁶ *Enterococcus faecium* was also found to antagonize *Giardia* infection in mice.⁷ In other research the administration of *Enterococcus faecium* reduced levels of *Clostridium* spp.⁸, *Staphylococcus*⁹ and *Pseudomonas*⁹ in dogs. Another study was recently presented that demonstrated the detection of one or more strains of a multistrain probiotic in 10 out of 12 dogs and 11 out of 12 cats administered the product as well as suggested that the probiotic product did not interfere with the interpretation of markers of gastrointestinal function.¹⁰

Data and scientific studies firmly documenting the benefits of probiotics in animals may be far fewer than on the human side, but given the huge interest and flurry of proposed research and pending results on veterinary studies-in-progress, that should be quite different in the near future. A similar situation occurred with the use of the joint supplements glucosamine and chondroitin sulfate, which went from initial hesitation to alternative medicine to mainstream therapy in a relatively short period of time, as positive research accumulated.

Yeast as a probiotic in horses

In human medicine, the yeast *Saccharomyces boulardii* (a subtype of *Saccharomyces cerevisiae*) is being investigated as a probiotic for treatment or prevention of diarrhea.^{11,12} *Saccharomyces boulardii* is a nonpathogenic yeast that has been used as an antidiarrheic agent in Europe¹³ since 1962 and in the United States.¹⁴⁻¹⁹

The mechanism of action of *S. boulardii* in cases of colitis in people caused by *Clostridium difficile* appears to be associated with the release, by the yeast, of a protease able to digest *C. difficile* toxins A and B.²² In addition to another proposed mechanism of action of an immunoprotective effect,^{23,24} the yeast has also been found to have adhesion sites for some strains of *Salmonella typhimurium* and *Escherichia coli* and may be useful in the treatment of enteric infections caused by those organisms.²⁵ In veterinary medicine, the use of *S. boulardii* has been associated with the poultry industry (decreases the frequency of cecal colonization by *Salmonella* spp in broiler chickens experimentally challenged after transport stress).^{26,27}

Although *S. boulardii* is not a normal inhabitant of the gastrointestinal tract in horses²⁸, the safe and therapeutic use of *S. boulardii* in horses as a probiotic has generated considerable interest because it can survive in the equine gastrointestinal tract after PO administration and does not permanently colonize the gastrointestinal tract (it is rapidly eliminated after oral administration is discontinued).²⁹ While additional controlled

studies are required to further assess the use of *S boulardii* as a therapeutic and prophylactic antidiarrheic agent in horses, a recent prospective study showed that in horses with acute enterocolitis, the severity and duration of clinical signs during hospitalization were significantly decreased in horses receiving *S boulardii*, compared to those receiving the placebo.²⁹ The authors of the study also suggested that it may be more effective to administer anti-diarrheal medication plus *S boulardii* than anti-diarrheal medication alone.²⁹ Research in other species suggests that *S boulardii* may be of benefit after colic or other intestinal surgery to support intestinal function.³⁰

The yeast *Saccharomyces cerevisiae* itself has probiotic properties; it helps protect against gastrointestinal imbalances in horses by stimulating activity of fiber-digesting bacteria in the hindgut. This leads to improved digestibility of nutrients (more available energy), especially important in mares, foals, and horses involved in competition and/or under any sort of stress.³¹⁻³⁴ *S cerevisiae* also has been shown to help maintain cecum and colon pH^{35,36} for optimal microbionics balance in horses.

Horses are notorious for the development of gastrointestinal issues, many cases of which are of undetermined etiology and may pose life-threatening complications. Treatment is often supportive (fluids, colloids, antidiarrheic agents, nonsteroidal anti-inflammatory medications), with or without antibiotics. The use of *S boulardii* and *S cerevisiae* as innovative biotherapeutic agents in horses with diarrhea to help reestablish and maintain gastrointestinal health has great promise, and should be considered as an adjunct to traditional therapy.

When to use probiotic supplements

The following examples of indications for the use of probiotics are by no means exhaustive but rather reinforce the potential benefits across a wide range of medical issues for which owners often seek evaluation and relief for their dogs and cats.

Stress-related gastrointestinal upset

Probiotics may be useful when dogs and cats are experiencing stress in general and stress-related diarrhea in particular as when boarding, traveling, in foster care or in shelters as well as during any sort of competition or change of environment.

Antibiotic-associated diarrhea

Probiotics may be indicated in dogs and cats receiving antibiotics as antibiotics may adversely affect the microbionics balance in the digestive tract resulting in diarrhea. Probiotics and antibiotics may be used together, although the two compounds should be administered at different times.

Dietary change or indiscretion

Another common cause of diarrhea in dogs and cats is dietary indiscretion or a sudden change in diet. Probiotics may be used to restore the population of beneficial bacteria, thereby mitigating the diarrhea.

For digestive tract microbiota imbalance

Food sensitivities, intolerance or maldigestion in animals can result in gastrointestinal upset; administering probiotics may be effective to address a digestive microbiota imbalance.

Weaning

Probiotics are often recommended to encourage healthy guts in puppies and kittens during weaning, smoothing the transition to solid-food diets.

Encouraging healthy bacteria and discouraging translocation of harmful bacteria

Many disorders are the result of harmful microbes. Including probiotics as part of a balanced therapeutic plan encourages the growth of beneficial bacteria and decreases the amount of harmful bacteria available to potentially translocate to other sites, for example the urinary or vaginal tracts as well as the liver and lungs.

Immune-mediated gastrointestinal conditions

Immune related gastrointestinal conditions may benefit from the use of probiotics, as probiotics can redirect misguided inflammatory responses from the immune system.

Recommended administration amount

A recommended administration amount is between one billion and ten billion CFUs per day per patient, regardless of the patient's weight (check the label of each particular probiotic supplement for details of the number of organisms it contains).

Precautions

Probiotics should not be administered to patients that are severely immunocompromised, due to concerns about the potential weakened integrity of the gastrointestinal mucosa.

Evaluation guidelines for choosing a probiotic

As with the evaluation of any supplement, there are a number of considerations including safety, stability and quality.

Safety studies should prove that the probiotic does not transmit antibiotic resistance to other microbiota and does not produce pathogenic factors. Because commercial probiotic products can become contaminated with other bacteria, a good probiotic contains only the organism(s) listed on the label.¹⁰ Probiotics must be able to survive in the gastrointestinal tract but be noninvasive and nonpathogenic.

Stability studies should document that the probiotic survives the manufacturing process, shipping, and recommended storage conditions. Because probiotics contain live microorganisms, keeping them stable (alive!) before use by the patient is one of the biggest hurdles to producing an effective probiotic. Manufacturers should ensure that an effective concentration of live probiotic microbes remains in the product at the end of its shelf life.⁴ All good products should carry a label claim (type and amount) of live bacteria with a specific expiration date.

Ease of administration and palatability are other issues that should be investigated before choosing a probiotic product.

Veterinary professionals interested in probiotic products are encouraged to seek out major manufacturers with stringent manufacturing standards and to scrutinize probiotics as they would any treatment option.

Embracing The Natural Forces Within

Probiotic therapy is in the spotlight for use in veterinary patients because of the substantial amount of research documenting positive benefits in a variety of species as well as the availability of commercial veterinary synbiotic products from reputable manufacturers.² The use of beneficial microbes offers veterinary professionals an exciting and timely adjunctive tool in the multi-modal management of gastrointestinal conditions and the overall support of the immune system and the digestive tract.

Key words: probiotic, prebiotic, gastrointestinal, digestive, *Enterococcus*, bacteria, microbes, microbiotica

References available upon request.