OPPORTUNITES FOR NON-NUTRITIONAL FEED ADDITIVES IN EXOTIC ANIMAL NUTRITION

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Introduction

Non-nutritional feed additives are substances, preparations, and micro-organisms that are added to animal feeds to improve animal health and performance. They may impact the immune system, endocrine system, receptor sensitivity, microbiome, and gut health, among other things. They are not designed to be a source of nutrients to the host animal but may provide nutrients to the microbiome.

Key categories of feed additives currently used in the animal space include prebiotics, probiotics, enzymes, fatty acids, phytogens, and novel compounds. Application is typically through animal feed or water, but recent research has led to products that may be applied intranasally or directly on the skin.

Feed additives have been extensively studied in domestic livestock. The use of feed additives in exotic animal nutrition is still in its infancy. However, captive exotic animals may benefit extensively from feed additives, as they may provide value in prevention or treatment of common diseases.

Loomis (2006) cites the most common medical problems encountered in zoos to include acute or chronic gastroenteritis, traumatic injuries, localized or generalized bacterial infections, parasitic infestations, obstetric problems, lameness, arthritis, and gastrointestinal foreign bodies. In addition, metabolic and degenerative diseases related to age and environment are present extensively in captive exotics (Terio *et al*., 2018).

As we consider the variety of gastrointestinal, infectious, and metabolic diseases in captive exotics, feed additives may provide value as a tool to either a prevent or treat disease. Their use, along with a high-quality diet, proper housing, and practical veterinary care, may aid in the reduction of disease. Therefore, the purpose of this review is to provide a brief overview of common feed additive types and their potential application in captive exotic animals.

Discussion

Prebiotics

Prebiotics are non-viable food components, mostly fibers, which confer a health benefit to the host (Pandey *et al*., 2015). Definitions often indicate that prebiotics modulate the microbiome; however, research suggests prebiotics also have an immunomodulatory effect (Broadway *et al*., 2015).

Common prebiotics used in food animal production include mannan-oligosaccharides (MOS), beta-glucans, and fructo-oligosaccharides (FOS) sourced from *Saccharomyces cerevisiae* yeast extract (yeast cell wall; Broadway *et al*., 2015). Several feeds also provide a source of prebiotics including breast milk, raw oats, and unrefined wheat and barley (Pandey *et al*., 2015).

Yeast cell wall components directly and indirectly interact with pathogens and components of the immune system. Research suggests they are involved in the release of cytokines including TNF-α, IL-1, IL-2, and IL-6. Beta-glucans have been shown to increase the functionality of macrophages and neutrophils (Broadway *et al*., 2015). The MOS component of yeast cell wall also binds directly to pathogenic bacteria such as E. coli, Salmonella, and Listeria through mannose-specific fimbria. This provides competitive binding sites for intestinal pathogens (Broadway *et al*., 2015; Heinrichs *et al*., 2003).

In domestic cattle, yeast cell wall products have been reported to reduce the impact of heat stress, improve the acute immune response during a lipopolysaccharide challenge, and reduce morbidity during respiratory disease or diarrhea events. Swine immune system and cytokine production may be stimulated at an earlier age with the use of yeast cell wall (Broadway *et al*., 2015). In dairy calves, probability of scours presence and severity was reduced with the use of a MOS product relative to control calves. The improvement in scours for calves fed MOS was similar to calves treated with an antibiotic (Heinrichs *et al*., 2003).

In captive exotic animals, their may be a benefit to using prebiotics during periods of stress to reduce the incidence of disease. Times of interest for use of prebiotics may be before and after transport, during gestation and the birthing period, during new animal introductions, and during outbreaks of disease. There also may be a great benefit to using prebiotics in the diets of young animals to reduce incidence of disease through activation of the immune system and pathogen inhibition.

Research in humans suggests value in prebiotics for reducing inflammatory bowel disorders such as inflammatory bowel syndrome (IBS) or inflammatory bowel disease (IBD). This may be achieved through modulation of mucin production and alteration of SCFA in the lower gut. There is some research to suggest prebiotics may also have a hypeprcholesterolemic effect. They may also be beneficial in the management of obesity, as they have a positive impact on the microbiome (Pandey *et al*., 2015). Based on data in humans, there may be a benefit to using prebiotics for the treatment or management of gastrointestinal diseases and metabolic diseases.

Probiotics

Probiotics are non-pathogenic organisms which provide a beneficial effect to the host (Pandey *et al*., 2015). Definitions vary as to whether these products need to contain viable cells or if they can contain non-viable cells. Common probiotics used in animal production include bacterial direct-fed microbials (DFMs) and yeast-based products.

Probiotics have been shown to stimulate the immune system, competitively exclude pathogens in the gut, detoxify undesirable compounds, shift VFA production, act as a source of micronutrients for microbes, produce antibacterial compounds, and product or stimulate enzyme production (Khan *et al*., 2016; McAllister *et al*., 2011; Pandey *et al*., 2015).

Research in ruminants has shown beneficial effects of probiotics on rumen microbial growth, reductions in rumen lactate, improvements in rumen pH, and improvements in rumen wall development (Chaucheyras-Durand *et al*, 2007; McAllister *et al*., 2011). In both ruminants and non-ruminants, probiotics are particularly beneficial for their ability to competitively exclude pathogens and stimulate the immune system (Cho *et al*., 2011; Dhama *et al*., 2011). Data in swine also suggest they may have a positive effect on nutrient digestibility.

In humans and companion animals, data suggests probiotics may be valuable for reducing incidence and severity of diarrhea and constipation and for reducing symptoms associated with gastrointestinal disease (IBS, IBS, etc.). They have also been shown to be beneficial for minimizing symptoms associated with allergies, respiratory disease, and urinary tract infections. Like prebiotics, probiotics have also been shown to have a hypeprcholesterolemic effect (Grześkowiak *et al*., 2015; Pandey *et al*., 2015).

There are an extensive number of probiotics currently available on the market with a range of data on each. The difficulty in applying probiotics in exotic animal diets will be identifying a probiotic with extensive replicated data. Yeast products are the most well studied in animals currently, but more data is emerging on bacterial DFMs. The best application for these products zoos may be with non-human primates experiencing gastrointestinal inflammation, as extensive data exists around the use of DFMs in humans with diseases such as IBS and IBD. Yeast-based products may be valuable in ruminants experiencing issues with rumen health. Probiotics may also be more generally applied in situations where immune stimulation may be beneficial such as during periods of stress or disease.

Phytogens

The term phytogen refers to plant-based compounds such as saponins, tannings, and essential oils. Common phytogens used in the animal feed industry include extracts from garlic, anise, cinnamon, oregano, yucca, and red pepper. On feed labels, they will commonly be referred to as "natural flavorings." This makes it particularly difficult to identify which phytogens may be in a specific feed additive.

Phytogens are most noted for their use as antiseptics and antimicrobials (Calsamiglia, 2007). The antimicrobial activity of phytogens is primarily driven by the phytogen interacting with the cell membrane. It is expected that phytogens will be more effective against gram-positive microbes due to improved cell membrane access. Antimicrobial activity of phytogens is typically observed when they are used at high doses (Calsamiglia, 2007).

In ruminants, changes in rumen VFA profiles and protein metabolism may be observed. In both ruminants and non-ruminants, bacterial and protozoal inhibition is the primary impact of high doses of phytogens (Calsamiglia, 2007).

Phytogens have a variety of impacts on health and have been shown to have a positive effect on cardiovascular disease, tumors, inflammatory processes, and diseases related to uncontrolled proliferation of free radicals. At lower doses, phytogens have been observed to impact pancreatic and small intestine digestive enzyme secretion, alter blood flow, have a hypocholesterolemic effect, and support gut health (Hagg *et al*., 2013; Platel and Srinivasan, 1996; Srinivasan, 2016).

Phytogens are difficult to implement in new animal species due to variability in products on the market, as well as lack of data on many available phytogens. However, they have the potential to be used to prevent disease, treat infection, or support metabolic health. Nutritionists and veterinarians interested in the application of phytogens should review the literature extensively to identify the best source and dose of phytogens of interest before applying them. Negative impacts of specific phytogen sources should also be considered, as some species will be more sensitive to specific phytogens.

Other Additives

Exogenous enzymes are used extensively in livestock production to support feed digestibility (Beauchemin *et al.*, 2003). There may be application for exogenous enzymes in captive exotic animal diets to enhance nutrient availability in poor quality diets. There is also potential for the development of novel enzymes with more specific targets in the gut related to health or microbiome function.

Short-chain fatty acids (SCFA) and medium-chain fatty acids (MCFA) may have value in enhancing the immune response and reducing pathogenic bacteria in animals (van Gerwe *et al.*, 2010). In ruminants, data suggests they may alter VFA production and protozoal populations (Hristov *et al.*, 2004). They may also impact neutrophil apoptosis during periods of stress (unpublished). Given the value of SCFA and MCFA in enhancing the immune response, they may be a valuable tool to reduce severity of disease or to prime the immune system for a stressful event.

Novel compound, including egg antibody products, quorum sensing products, and novel proteins among others, are also under review in livestock and humans. The benefit of many novel compounds is their ability to be used in a targeted manner. For example, 3- nitrooxypropanol (3-NOP) is a compound specifically developed to inhibit a key enzyme in the molecular pathway for methane production in ruminants (Hristov *et al.*, 2015). Another example is sucram, a high-intensity sweetner, which directly impacts glucose receptor activity in the gut leading to improved gut health and glucose uptake (Connor *et al.*, 2015). Other products directly influence specific microbial communities or target specific types of pathogens. This area is expected to grow with the use of new technology for creating and identifying compounds of interest.

Blends are also being created which take advantage of the comprehensive modes of actions of several compounds to hit multiple targets in an animal. For example, a probiotic and phytogen blend may stimulate the immune system while also improving the structure of the gut lining leading to a dual impact on an animal with leaky gut.

Conclusion

An extensive array of feed additive products exists in the current market. Use has been primarily in humans and domestic animals, but there may be a benefit to using additives in captive exotic animals. With an array of different species zoos, it will be critical for nutritionists and veterinarians to fully understand the feed additive products available to them, the modes of action of those products, and the potential interactions of those products with other additives, dietary ingredients, and medications. To help make these decisions, more data needs to be collected in zoological institutions on animals facing a risk of illness and disease.

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