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Prebiotics and Synbiotics in Equine Health and Disease

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Abstract

Prebiotics are non-digestible food ingredients that promote the growth of probiotic microorganisms in the intestines. They are marketed as feed supplements to support equine digestion, metabolism, growth, and immunity. Synbiotics are supplements that contain combinations of prebiotics and probiotic bacteria and/or yeasts. Both prebiotics and synbiotics are commercially available and are promoted for use in supporting equine digestion, enhancing athletic performance, as well as reducing stress and morbidity associated with intestinal disease. This narrative review aimed to summarize the literature on the use of prebiotics and synbiotic supplementation in equine nutritional practice. Sixteen papers were identified that reported on the use of prebiotic or synbiotic supplementation in horses. The literature presented here suggests that prebiotics may play a role in equine health and disease prevention. Prebiotics have been studied for their effects on athletic performance; increasing production of volatile fatty acids (VFA's) associated with hindgut fibre fermentation; insulin resistance and carbohydrate metabolism associated with reduction in the development of gastric mucositis, and hindgut acidosis and laminitis. Prebiotic compounds are thought to have an entero-protective effect by improving the composition and diversity of the intestinal microbiota, that in turn impacts immune function via metabolomic effects. Prebiotics derived from yeasts, including mannan-oligosaccharides (MOS), have been shown to reduce colonies of intestinal pathobionts and accelerate healing in acute enterocolitis. Overall, the current evidence to support the use of prebiotics and synbiotics in equine health and disease is not extensive but promising.

Keywords

Equine; prebiotics; fiber; synbiotics; microbiome; digestion

1. Introduction

Equine veterinarians play an important role in advising on interventions that prevent and treat gastrointestinal disorders in horses. Equine gastrointestinal disorders include scouring in neonates [1], colitis and fatal colic events [2], parasitic gastrointestinal infections [3], gastric ulceration [4], salmonellosis associated inflammatory bowel disease [5], coronavirus infection with necrotizing enteritis and eosinophilic enterocolitis [5], sand-accumulation enteropathy [6] and caecal disorders [7]. Dysbiosis of the intestinal microbiome defined as "a loss of diversity, a bloom of potential pathobionts, and a loss of commensals" [8] may predispose horses to many of these gastrointestinal disorders [9]. Interestingly, there is evidence to suggest that equid type (size, breed, or conformation) may influence predisposition to the development of various gastrointestinal lesions; for example, larger breeds such as Clydesdales experience more caecal disorders, whereas smaller breeds and miniature horses are less likely to be affected by colon displacements [10]. Furthermore, extraintestinal conditions such as exacerbations in asthma [11], obesity [12], and impaired athletic performance [13] have all been associated with alterations to the composition and diversity of the equine gastrointestinal microbiome. Therefore, the equine microbiome has gained increasing attention in veterinary research [14] as reflected by the initiation of the Equine Gut Microbiome Project in 2015 [15].

Hindgut fermentation, which fundamentally influences intestinal microbiome composition [16,17], is a digestive process seen in animals with a simple, single-chambered stomach. These animals include equids, rhinoceros, koalas, rodents, and rabbits; in these mono-gastric herbivores, cellulose from plant foods is digested with the support of intestinal bacteria [18]. Popular interventions thought to alter the composition and diversity of the gastrointestinal microbiome include supplementation with probiotics and prebiotics. Probiotics are defined as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" [19] and prebiotics are defined as "selectively fermented ingredients that result in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health" [20].

Prebiotics are widely used in equine management regimens to support the intestinal processing of a variety of feedstuffs, based on the belief that they improve the diversity and richness of the species that inhabit the intestinal microbiome [21]. Adding prebiotics containing fructo-oligosaccharides (FOS) or mannan-oligosaccharides (MOS) to high-fiber diets increases feed digestibility, supports energy production, and improves the general fitness and health of the horse [21]. Research conducted with Irish thoroughbreds undergoing a sudden change in feeding regimen found that digestive sensitivity particularly affected individuals carrying a limited abundance of hindgut core bacterial species [22].

When probiotic bacteria and/or yeasts are combined with prebiotics, the formulation is referred to as a 'synbiotic'. These combinations have been used in human studies to promote the growth of beneficial microbes, aiming to increase the diversity and richness of the intestinal milieu [23].

While there are limited studies in the equid, the potential role of pro- and prebiotics in human health and disease has been explored far more extensively, with the current PubMed citations exceeding five thousand. No summary of studies that report on the nutritional and therapeutic role of prebiotic and synbiotic supplementation in equine health and disease has been conducted to date. Therefore, the aim of this review was to provide an overview of the literature reporting on the use of prebiotic and synbiotic supplements, in equine nutritional practice. An online search of Embase and PubMed databases for papers published from inception to 2023, using the search terms 'prebiotics', 'synbiotics', 'horses', and 'equine', was conducted to identify original research evaluating the effects of prebiotics and synbiotics on the composition and/or metabolism of the equine intestinal microbiome, along with associated health outcomes.

Sixteen papers reporting on the effects of prebiotic or synbiotic supplementation in horses were subject to full-text review. The findings of those studies are discussed and evaluated here. This review does not address the use of probiotics in equine populations, which was the topic of a previous review published by the authors of the present manuscript [24].

2. Types of Prebiotics

In the horse, naturally occurring prebiotic compounds can constitute part of the regular feed or supplementation regimen, supporting potential colonization of the intestinal environment with bacteria that are thought to confer a benefit. Prebiotics include fermentable sugars, predominantly oligosaccharides or disaccharides, of which there are several types: oligofructose, inulin, isomalto-oligosaccharides (IMOS), lacto-sucrose, fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), lactulose, pyrodextrins and xylo-oligosaccharides (XOS), and mannan-oligosaccharides (MOS) [25]. Certain prebiotic types are compounded dietary sugars, for example, FOS is composed of short chains of fructose molecules and GOS is composed of a chain of galactose molecules; IMOS is derived from the disaccharide maltose (sourced from honey, for example) following enzymatic activity, which produces a mixture of short-chain carbohydrates; XOS, a natural prebiotic fiber extracted from sugar cane fiber, and inulin belong to a class of polysaccharides known as "fructans" and are found in vegetables such as Jerusalem artichoke, plantains, and chicory root. MOS are complex carbohydrate molecules, derived from the outer cell wall of the yeast *Saccharomyces cerevisiae* - mainly β-glucans (mannoproteins). Soluble arabinogalactans are classified as non-carbohydrate sources of prebiotic fiber derived from larch trees (*Larix sp.*) [26]. From the literature, equine prebiotics most studied are inulin, FOS, GOS, and MOS.

Different prebiotic classes supply fuel to resident microbes in various regions of the equine gut. The caecum and colon comprise 66% of the digestive tract volume and contain large populations of anaerobic bacteria; these probiotic species process pectin, cellulose, hemicellulose, and starch, producing volatile fatty acids (VFA's) through the process of fermentation, to be utilized as a metabolic energy source [27]. The hindgut (colon and caecum) houses a complex microbiome, composed of mostly bacteria but also viruses, fungi, protozoa, archaebacteria, and phages; these microorganisms ferment the residual indigestible cellulose which has not been processed proximally, to produce VFA's that serve as a fuel source for the host [28]. Nutrients including protein and B-group vitamins are also rendered more digestible by microbial fermentation in the hindgut [21]. Equids digest a very limited amount of the lignin present in plants, and it is mostly excreted in feces, as they lack the necessary enzymes, relying on microbially-generated enzymes to aid digestion [29].

3. Prebiotics in Forage and Carbohydrate Digestion

Forage of various types supplies energy, nutrients, and prebiotics to equids; by definition, the prebiotic constituents of regular feed assist in promoting the growth of intestinal microbiota that confer a health benefit [30]. Naturally occurring fructans are long-chain sugar molecules found in a variety of pasture grasses, with nutrient-dense verdant grasses being higher in fructan content and ranging to low-fructan native grass species, the latter being prevalent in Australia [31]. While fructans are considered to act as prebiotics, grass varieties such as Timothy and some types of Perennial Rye are either processed rapidly in the equine intestine or have a significant proportion of their carbohydrate pass undigested into the hindgut for fermentation by resident microbiota, generating lactic acid as a by-product [31]. Contrary to the definition of a prebiotic, high fructan intake is thought to contribute to the development of hindgut acidosis, increasing the risk of laminitis [32], however, this effect may be ameliorated by the addition of different prebiotic fibers to the feed which degrade more slowly [33]. Mature grasses are composed of more indigestible fiber [34] and fewer fructans than young fresh grasses, hence presumably would pose less risk of hindgut acidosis to horses grazing on these pastures. From a management perspective, grazing horses on native grasses is preferable to administering prebiotic extracts, as native grasses are more fully processed and do not contribute to increased intestinal gas production which might arise from unfermented fructans reaching the hindgut [31].

The starch component of an ideal equine prebiotic feed should predominantly degrade in the intestine, proximal to the hindgut. Jerusalem artichoke is a source of the prebiotic FOS and inulin, which can influence the metabolism of hindgut microbiota by modulating the fermentation of ingesta [21]. Additionally, according to one study in which carbohydrate processing from the stomach to the transverse colon was evaluated, Jerusalem artichoke can also contribute to increased gas production in the hindgut due to the fermentation of undigested fructans [33]. Importantly, inulin derived from Jerusalem artichoke is fermented differently than that present in grasses and may not support the development of beneficial *Lactobacillus* colonies as effectively as the inulin from forage does. The rapid fermentation of high fructan grasses favors hindgut cultivation of lactate-producing bacterial species, such as *Streptococcus bovis* and *S. equinus*, overwhelming colonies of predominantly lactate-utilizing species, such as *Veillonella sp.* and *Megapshera sp.*, the latter which metabolize lactate to propionate [32,35,36]. If carbohydrates ferment early in their passage through the equine foregut (esophagus, stomach, and small intestine), rather than having this process slowed by the presence of indigestible prebiotic fiber, the resultant production of organic acids may accumulate and produce mucosal injury (ulceration) [33]. An *in vivo* experiment conducted on postmortem equine gastric mucosa tissue samples, applying various concentrations of butyrate to replicate those achieved by natural Jerusalem artichoke bacterial fermentation in the hindgut, showed evidence of injury to the gastric mucosa, postulating that this FOS-rich prebiotic supplement could increase the risk of developing equine gastric ulcer syndrome (EGUS) [37].

4. Prebiotic Supplementation in Hindgut Fermenters

Given the limited literature relating to the use of prebiotic supplementation in horses, it is of interest to consider what is known about other species that are hindgut fermenters. Researchers have explored the effects of supplementing the diets of other hindgut fermenting animals with prebiotics, specifically rodents and rabbits. These studies found associated improvements in lipid metabolism, the composition of the intestinal microbiome, and nutrient absorption, particularly minerals [18]. Hindgut fermentation, cell-mediated immunity, and various blood parameters improved in rats supplemented with pulverized Jerusalem artichoke, rich in prebiotic inulin and FOS for twelve weeks [38]. Further, in these rats, skin indurations induced by a mitogen reduced, while CD4 lymphocyte populations increased, and blood levels of glucose, urea, and hemoglobin in these rats adjusted favorably [38]. Yeast-derived MOS supplementation enhanced VFA concentrations and lowered pH in the cecal region of rabbit intestines and was associated with longer intestinal villi when compared to controls. In addition, the weight gain observed with the addition of MOS to the diets of the study animals was similar to that which could be expected from antibiotic treatment for promoting growth [39]. By further comparison, koalas possess a proportionally large hindgut for processing their exclusive diet of Eucalyptus leaves and, while their core intestinal microbiome has been explored [40], no study has been published involving prebiotic supplementation of this marsupial species nor the other remaining hindgut fermenter, the rhinoceros. Although evidence supporting the use of prebiotics in the dietary management of horses is limited, there are many commercial prebiotics and synbiotic supplementary feed formulations, currently available in several countries, which are purported to enhance the intestinal microbiome, digestion, energy production, and immunity.

5. The Effects of Prebiotics on the Equine Microbiome

There is a paucity of studies evaluating how the addition of prebiotic compounds to commercial horse feeds impacts the intestinal microbiome. Most attention has been given to the modulation of intestinal carbohydrate processing by specific prebiotics to reduce the incidence of laminitis, which can be experimentally induced by administering large doses (10g/kg bwt) of fructans to horses [41,42]. Such carbohydrate loading causes acidification of the intestinal milieu, producing a shift from eubiotic Gram-positive bacteria to lactate-producing species, such as *Streptococcus bovis/equinus* in the gut microbiome [32]. It is believed that these bacterial species, via the generation of vasoactive amines and endotoxins which can permeate into the systemic circulation and cause ischemia/reperfusion injury to the equine digit, contribute to the development of laminitis in horses [42]. A balance needs to be maintained between the number of commensal bacterial species which are lactate-producers (e.g. *Lactobacillus salivarius*, *L.delbreukii*, *L. mucosae*) and those which are lactate-utilisers (e.g. *Veillonella sp.*, *Megasphera sp.*) [36]; the latter metabolize lactate to propionate to support energy production, with propionate being a key precursor molecule for gluconeogenesis [43].

Prebiotic sugars and fibers provide energy and nutrients to intestinal microbiota to fuel their metabolic activity. Berg *et al.* evaluated supplementing the diet of yearling quarter horses with FOS, finding that this intervention led to alterations in the microbiome and metabolome, with respect to fecal pH and concentrations of VFA's [44]. These researchers reported a quadratic effect on fecal *Eschericia coli* populations following FOS supplementation without any apparent alteration in the numbers of *Lactobacillus sp.*; fecal propionate, butyrate, acetate, and lactate concentrations increased linearly with total VFAs in this study [44]. Such VFA's generated by intestinal microbiota can provide an additional energy source to carbohydrates for athletic performance in trotting horses.

Hence, providing such prebiotics to generate fuel could be considered performance-enhancing supplementation.

In Warmblood horses fed FOS and inulin supplements daily for 3 weeks, the abundance of *Lactobacillus sp.* increased in relation to that of *Streptococcus sp.*, which decreased in the gastric microbiome, while higher alpha diversity of the intestinal microbiome was observed **[45]**. Alpha diversity refers to the number of species (species richness) within that region. Fructo-oligosaccharides are thought to support the colonization of the equine intestine with *Bifidobacteria*, although the effect of this increased colonization is not fully understood **[30]**. There is limited evidence for the function of *Bifidobacteria* in the equine gut microbiome, which contains a much larger proportion of *Lactobacilli*, even in relation to that found in humans, however, these indigenous probiotic bacteria do not typically utilize FOS as consistently as do *Bifidobacteria* **[30]**.

The core intestinal equine microbiome is considered to be healthy if it contains a relative abundance of *Firmicutes* with respect to *Bacteroidetes* phyla **[9]** and specifically it is the metabolic function of the intestinal microbes which determines equine health. The fecal microbiome composition of ten healthy horses following supplementation with prebiotic cellobiose for 14 days was profiled by Paßlack *et al.*; the relative abundance of *Firmicutes*, *Coriobacteriales*, and *Clostridium* increased in a dose-dependent way, with a dose-dependent decrease in the relative abundance of *Bacteroidetes* **[46]**. By association, these findings suggest an improvement in the composition of the fecal microbiome of the study horses following the administration of prebiotics.

Yeast-derived prebiotic and postbiotic compounds, derived from the fermentation of *S.cerevisiae* and administered as feed topdressing to a cohort of Quarter horses in a recent study, have been shown to stabilize the composition of the intestinal microbiome following a stress event **[47]**. These entero-protective supplements were also found to modulate the early immune response favorably in 11 English Thoroughbreds following vaccination against equine influenza **[48]**.

By promoting a healthy balance between species in both the major and minor phyla of the intestinal microbiome, prebiotics support the condition of the gut mucosa, enhance nutrient absorption and athletic performance and overall equine health **[49]**. Antibiotic use can be significantly reduced by supplementing livestock and companion animals with synbiotics **[49]**, however, such benefits have not yet been shown in equine management **[30]**.

6. The Effects of Prebiotics on Equine Health and Disease

Table 1 shows the selected publications for review concerning the effects of prebiotic or synbiotic supplementation in horses.

6.1. Equine Performance

Exercising horses are often fed high carbohydrate, grain-dominant diets to deliver immediate energy for enhanced performance. This practice reduces natural forage intake, placing these athletes at risk of developing hindgut acidosis and possibly intestinal dysbiosis, a condition which may also be stress-induced **[50]**, and which has been observed in cattle fed high carbohydrates **[51]**. The prebiotic fiber found in sugar beet is thought to offer a glycogen-sparing effect when added to such feed, due to enhanced propionate production by intestinal microbiota, thereby assisting energy production for performance **[52]**. During intense exercise in standardbred geldings, increased concentrations of muscle glycogen, lower muscle lactate levels, and lower peak plasma lactate concentrations were found following supplementation of their standard diet with sugar beet pulp. This effect was attributed to additional VFAs being utilized for aerobic energy production instead of glycogen **[52]**. High prebiotic fibre-containing diets supply equivalent amounts of energy via glycogen and propionate production compared to lower prebiotic, high-carbohydrate, grain-based diets, also delivering a beneficial alkalizing effect to protect against lactic acidosis generated by intense exercise **[44]**. These findings could inform equine athlete management for protection against dietary complications and consequent illness, whilst improving performance in these horses.

6.2. The Effects of Prebiotics on Equine Glucose Regulation and Insulin Resistance

Polyphenols and fibers with prebiotic properties have been proposed to reduce inflammation in senior horses possibly via improvements in insulin resistance **[53]**. Improved glucose metabolism is thought to occur via metabolomic effects including an increase in butyrate **[54]**. In humans, a lower abundance of butyrate-producing intestinal bacteria has been associated clinically with a higher incidence of Type 2 diabetes, in comparison to healthy controls unaffected by intestinal dysbiosis **[55]**.

Supplementing the standard crushed oat and meadow hay diet of six healthy Warmblood mares for 21 days with Jerusalem artichoke meal, providing prebiotic FOS and inulin, produced a rapid serum insulin peak, followed by a faster decline of both glucose and insulin when compared to controls; this effect was associated with the relative abundances of *Lactobacillus* increasing and *Streptococcus* decreasing in the stomach of the prebiotic-fed group **[56]**.

These findings also suggest a potential protective effect of this prebiotic (FOS and inulin) against insulin resistance/metabolic syndrome and obesity in these animals. High soluble carbohydrate in equine feed (grains and spring grass) increases the prevalence of insulin resistance and obesity, reducing the bacterial diversity of the intestinal microbiome and shifting its composition unfavorably towards potential pathogens such as *Streptococcus lutetiensis*, a species linked to the development of laminitis **[42]**. Supplementing the daily diet of eight obese mature Arab geldings with short-chain FOS over a period of six weeks optimized fiber processing which increased insulin sensitivity, while reducing acute insulin response to glucose and resting serum insulin, without altering body weight or body condition score **[57]**. Further, senior horses experience a decline in digestive capacity and the risk of developing insulin resistance increases with advancing age; supplementing the diet of older horses with FOS may improve the composition of the intestinal microbiome of these animals, resulting in better metabolic condition **[58]**.

Table 1: Selected publications on the effects of prebiotic or synbiotic supplementation in horses.

Author, Date, Country	Horses studied – sex, age, breed, health status	Intervention	Duration of study	Results
Berg *et al.*, 2005, USA [44]	9 Quarter horses	Diets supplemented with 8 g of FOS/d (low), or 24 g of FOS/d (high)	Three 10-day feeding periods	Fecal pH decreased and total VFA's increased linearly from control to low-FOS, then high-FOS diets. FOS supplementation altered fecal microbiomes, with a quadratic effect observed for *Escherichia coli* populations ($P < 0.01$)
Respondek, 2011, France [57]	8 obese mature Arab geldings (BCS = 8)	4 horses received maltodextrin 45 g/day/horse (control) and 4 horses received the same amount of short-chain fructo-oligosaccharides (scFOS)	Six weeks	Supplementation with scFOS increased insulin sensitivity and reduced acute insulin response to glucose and resting serum insulin in comparison with maltodextrin ($P < 0.05$), without affecting body weight or body condition score. No changes were observed in plasma glucose, serum leptin, or triglyceride levels ($P > 0.05$)
Adams, 2015, USA [59]	40 mixed breed and sex horses, age range 20–33	Four treatment groups: 1. Traditional grain mix; n=10 2. Control; n=10 3. Control + DHA; n=10 4. Control + ActivAge®prebiotic; n=10	Twice daily for 161 days All horses vaccinated on day 56 with equine influenza vaccine and a novel antigen (OVA) Vaccination was boosted on day 70	Serum cytokines TNF-α, IL-6, and IFN-γ were measured prior to and 2 weeks post-vaccination. All inflammatory markers reduced significantly in prebiotic supplemented group compared to horses receiving traditional grain mix, control diet only and DHA
Czech, 2006, Poland [60]	20 Thoroughbred mares	10g/d mannan oligosaccharides (Bio-Mos®)	20 days prepartum	Bio-Mos® improved blood antioxidant status but did not significantly alter the nutritional composition of mare's milk other than a slight protein increase. Treated mares had 20% higher RBC; 30% higher alkaline phosphatase and lactate dehydrogenase; 24% higher plasma superoxide dismutase than controls
Vendrig, 2014, The Netherlands [61]	10 Warmblood pony foals	6 foals supplemented orally with 15g Vivinal® syrup (GOS 45%, lactose 16%, glucose 14%, and 25% water), 4 foals were controls	Twice daily for 28 days from birth	No differences were observed between Vivinal® treated foals and the control group for the range of hematological parameters (hematocrit, white blood cell types, protein, albumin, and various immunoglobulins). *Ex vivo* LPS-induced mRNA expression levels of IFN-γ and IL-6 were significantly lower in PBMCs derived from treated foals compared to the control group
Vendrig, 2013, The Netherlands [62]	Peripheral blood mononuclear cells (PBMC) from 12 healthy Dutch Warmbloods	*In Vitro*	N/A	TNF-α production by PBMCs increased significantly at all oligosaccharide concentrations, compared to controls, with dose-dependent effects seen for all three fractions. Production of IL-10 in unchallenged PBMCs was not significantly influenced by GOS/FOS/AOS compared with blank controls. Several oligosaccharide fractions produced distinct direct immunomodulatory effects
Hassel, 2020, USA [63]	10 horses with radiographic presence of large quantities of sand	Assure® 15g/d or Assure Plus® 226g/d containing a custom blend of psyllium, prebiotics, probiotics, yeast, and digestive enzymes	35 days	Reduction in sand accumulation was observed in all horses, however, there were no significant differences between the treatment and control groups
Niinistö, 2020, Finland [64]	34 hospitalized horses	12 horses given psyllium 1 g/kg bwt only; 10 horses given $MgSO_4$ 1 g/kg bwt only; 12 horses given combined	Via nasogastric intubation daily for 4 days	A combination of psyllium and $MgSO_4$ cleared areas of sand accumulation significantly more ($P < 0.001$) than control horses

Author, Date, Country	Horses studied – sex, age, breed, health status	Intervention	Duration of study	Results
Landes, 2008, USA [65]	8 clinically healthy equids (5 horses, 3 mules, and 1 pony)	60g prebiotic/ probiotic, containing minimum 40 x 10^9 cells *Saccharomyces cerevisiae*, 2.25 x 10^9 CFUs *Lactobacillus acidophilus* and 1.55 x 10^9 CFUs *Enterococcus faecium* plus 0.5 g/kg psyllium	Daily for 35 days	Average fecal sand output for each horse was at least 2.5 times greater during treatment than in the pre-treatment period for all equids. Fecal sand output on days 1–3 was same as pre-treatment, then significantly increased and remained higher day 4–31
Glatter, 2019, Germany [45]	12 adult healthy warmblood horses	FOS + inulin from Jerusalem artichoke meal (JAM) 0.2 g/kg bwt/d	Daily for 3 weeks, then euthanized 1 hour after final meal	The relative abundance of *Lactobacillus* increased and *Streptococcus* decreased predominantly in the stomach of the prebiotic-fed group. Higher alpha diversity and richness of microbiota were seen in all regions of the GIT, particularly the large intestine, for subjects fed JAM compared to controls ($P < 0.05$). Similar beta diversity was seen in treated subjects and controls. More evenness of species was seen in small and large intestines of JAM-supplemented subjects
Bachmann, 2020, Germany [33]	12 adult healthy warmblood horses	FOS + inulin from Jerusalem artichoke meal (JAM) 0.2 g/kg bwt/d *In vitro*: Fresh digesta removed from selected regions of the GIT, and incubated anaerobically to measure gas production	Daily for 3 weeks, then euthanized 1 hour after final meal	FOS and inulin were mostly fermented in the stomach, not reaching the hindgut in significant quantities, indicated by increased gastric gas production. Stomach pH was lower and VFA concentrations higher in JAM-treated compared to control subjects, but similar in hindguts of both groups. Oxidation-reduction potential increased twofold from pre- to post-incubation with JAM
Cehak, 2019, Germany [37]	Gastric mucosa samples obtained from 3 healthy horses, euthanized	*In vitro*: Mucosal tissue samples treated with four butyric acid concentrations of 10, 18, 24 and 32 mmol/l	N/A	Tissue samples *in vitro* produced histopathological changes consistent with those observed in horses fed prebiotic JAM. The severity of mucosal injury increased with higher concentrations of butyric acid
Glatter, 2017, Germany [56]	Six healthy, warm-blooded mares (age: 6–13 years)	Standard diet (crushed oat grains, 1g starch/kg bwt/d with meadow hay 2kg/100kg bwt/d plus either 0.15g FOS and inulin /kg bwt/d via JAM or control (equal amount of maize cob meal)	2 × 21-day treatment periods	Feeding of JAM versus control resulted in a particularly rapid and definite peak of serum insulin, followed by a faster decline in both plasma glucose and serum insulin post-prandial. Plasma glucose returned to baseline most completely with JAM but not control
Bachmann, 2021, Germany [66]	12 Warmblood horses (10 females, 2 males)	6 horses received 0.15g FOS plus inulin/kg bwt/d via JAM 6 horses fed corncob meal without grains (placebo)	20 days, then euthanized	Simple sugars and fructans rapidly disappeared from gastric digesta at the postprandial state in prebiotic-supplemented horses; elevated degradation to lactic acid and SCFA, especially n-butyric acid, may have gastric and metabolic health impacts
Paßlack, 2020, Germany [46]	8 healthy adult horses, 2 ponies	10g cellobiose /d or 20g cellobiose /d	14 days	A dose-dependent increase in the relative abundance of *Firmicutes* ($P = 0.04$), *Coriobacteriales* ($P < 0.00$), and *Clostridium* ($P = 0.03$) detected. A dose-dependent decrease in the relative abundance of *Bacteroidetes* ($P = 0.03$)

FOS – Fructo-oligosaccharides; GOS – Galacto-oligosaccharides; AOS - Acidic-oligosaccharides; VFA – Volatile fatty acid; CFUs - Colony forming units.

6.3. The Effects of Prebiotics on Equine Intestinal Inflammation

The discovery that prebiotic supplements may modulate intestinal inflammatory and immune responses has potential applications for veterinary medicine. Anti-inflammatory and immunomodulatory activity have been demonstrated in two equine studies [59,62] and one human study [67] using prebiotics. Specific actions of microbial metabolites, such as butyrate, are believed to include reduced cytokine production by the mucosal cells lining the intestine [67]. Anti-inflammatory and immunomodulatory activity of prebiotics were demonstrated in one *in vitro* study, in which equine peripheral blood mononuclear cells (PBMCs) were challenged with lipopolysaccharide (LPS) to induce an inflammatory response [62]. A protective effect was observed when PBMCs were pre-incubated with GOS/FOS/AOS (acidic oligosaccharides) prior to being challenged with LPS, producing a dose-dependent reduction in both tumor necrosis factor alpha (TNF-α) and interleukin (IL-10) production. However, if PBMCs were pre-treated with GOS or GOS/FOS fractions alone, TNF-α production by the immune cells rose substantially [62]. These oligosaccharide fractions demonstrated a dampening effect on the allergic response while enhancing immune defenses in PBMCs; pre-treatment incubation with glucose/lactose concentrations similar to 1% GOS, as a comparison control, significantly increased cell viability by 14%, while GOS/FOS/AOS pre-treatment increased cell viability by a range of 38-61% [62]. The authors suggested that this protective effect on PBMCs was due to lower mitogenic potential [62].

7. Prebiotic Yeast Extracts in Equine Health and Disease

Mannan-oligosaccharides, derived from proteins in *S. cerevisiae* cell walls, protect against bacterial infection by competitively inhibiting the binding of bacterial lectins to intestinal enterocytes [68] and a dried yeast extract from mechanically ruptured *S. cerevisiae* cells containing beta-glucan acts as a prebiotic substance, effectively absorbing mycotoxins from contaminated feed and thereby offering immune protection [69]. In terms of the impact of prebiotic yeast extracts such as MOS on inflammation, horses exhibiting exercise-induced stress demonstrated more rapid recovery of cortisol and cytokine levels following eight weeks' supplementation with a fermented *S. cerevisiae* product as compared to controls [70].

Twenty thoroughbred mares supplemented with MOS, for 20 days prepartum, exhibited improved blood antioxidant parameters, namely 24% higher plasma superoxide dismutase levels than controls, without alteration to the nutritional composition of their milk [60]. Furthermore, there is evidence to suggest that mares' plasma and colostrum IgG levels may be boosted by adding MOS to their feed, protecting both mare and foal for 24 hours post-partum from serious infectious complications, such as diarrhea, sepsis, and possibly death [71].

7.1. Prebiotic Safety

It is generally considered that prebiotics may be safely administered to horses, although this assumed safety has not yet been scientifically evaluated. Any alteration in feed or supplementation which might adversely impact microbial diversity and species richness could disturb intestinal homeostasis [72]. Intestinal dysbiosis often results from the administration of antibiotics to horses and may render the animal susceptible to the proliferation of pathogenic species such as *Clostridium difficile* and *Salmonella sp.* in the gut, causing antimicrobial-induced colitis [73], and diarrhea [72]. Prebiotics have been shown to protect horses against intestinal dysbiosis, by supporting the colonization of favorable probiotic species and dispelling enteric pathobionts [36]. Soluble arabinogalactans, the prebiotic fiber derived from larch (*Larix sp.*) was administered to foals to treat scouring with some benefit and, although its specific mode of action is yet to be determined, its administration has proven to be safe in young horses [30]. Another study supplemented seven mares and their foals with a soluble arabinogalactan preparation (LaraFeed AC9) for 2 weeks pre-foaling and until 14 days post-foaling, using five mares and their foals as controls. The results were a lower frequency of diarrhoea episodes with more normal feces amongst the treated foals, requiring less veterinary intervention in comparison to controls. No treatment effects were found in the foals with respect to weight, blood parameters (complete blood count (CBC), immunoglobin A (IgA), and immunoglobulin G (IgG)), or fecal *Salmonella* or *Rotavirus* cultures, demonstrating tolerance for the larch extract [74].

8. Synbiotics in Equine Health and Disease

A combination of a probiotic and a prebiotic, referred to as a synbiotic, can increase the survival time and colonization potential of the probiotic bacteria or yeast in the intestinal milieu [30]. There is also some evidence that synbiotics may be beneficial for assisting intestinal sand clearance in horses, thereby playing a preventive role against the development of sand colic and enteropathy [65]. The accidental ingestion of sand commonly occurs in horses as a result of daily feeding on pasture grasses [65], which may result in sand accumulation and lead to colic. Synbiotic treatments containing probiotics (*Lactobacillus acidophilus*, *Enterococcus faecium*), prebiotics (derived from *S. cerevisiae*), and up to 90% psyllium seed husks have been effectively utilized to reduce and treat sand enteropathy and sand colic [65]. While sand accumulation was significantly reduced with this treatment, radiographic evidence of clearance was not observed [63]. It is uncertain, however, whether pre- and probiotics play a significant role in correcting this painful condition, or whether favorable results are achieved by dosing with high-fiber pulverized psyllium seeds alone. A synbiotic-only effect on this condition cannot be confirmed with this study, as the treatment contained predominantly psyllium seed husks, however, there may have been a therapeutic synergism delivered by the compound treatment formulation. Another report has been published on the more effective removal of accumulated intestinal sand with psyllium seed husk therapy supported by the addition of cathartic magnesium sulfate via nasogastric delivery [64].

The addition of probiotics to prebiotic supplementation has also been shown to assist in improving the composition of the equine microbiome [21] and provide protection against excess colonization of microbial pathogens, thereby reducing the requirement for antibiotic use [71]. A recent review reported on the safety, tolerability, and efficacy of probiotic bacteria currently in equine veterinary use, revealing conflicting evidence for the overall health benefits of probiotic bacterial treatments for horses, although some specific benefits for managing scouring in foals and improving athletic performance were reported [24]. In general, recent publications are supporting the use of prebiotics plus probiotics to improve animal health by manipulating the microbiome of many different domestic, livestock, and wild species, without the need for antibiotic use, thus providing societal and economic benefits [75].

9. Conclusion

Current evidence for the use of prebiotics and synbiotics in the management of equine health and disease is not extensive, although it could be considered promising and practical in many cases. Prebiotics and synbiotics, when added to the equine diet, have been shown to influence insulin sensitivity for obesity prevention, to reduce markers of systemic inflammation and allergy, and intestinal dysbiosis. Reduction of hindgut acidosis and correcting intestinal dysbiosis by the administration of prebiotics containing fiber to the equine diet may also confer protection against inflammatory conditions such as colitis and laminitis. Finally, the thoroughbred racing industry might consider adopting the safe and legal practice of administering prebiotics to their athletes, to assist energy production from volatile fatty acids resulting from microbial fermentation.

Authors' Contributions

CGC conducted the review of the literature, compiled the table of publications, and drafted the manuscript; JEH, ZG, and CGG reviewed the findings, revised the manuscript, and approved the final draft.

Data Availability

All data presented are published by the authors listed in this review.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethical Approval

Ethical approval was not required to conduct this review.

References

[1] Browning GF, Chalmers RM, Snodgrass DR, Batt RM, Hart CA, Ormarod SE, *et al*. The prevalence of enteric pathogens in diarrhoeic Thoroughbred foals in Britain and Ireland. Equine Veterinary Journal 1991;23:405–9. https://doi.org/10.1111/j.2042-3306.1991.tb03751.x.

[2] McConnico RS. Acute colitis in horses. In: Sprayberry KA, Robinson NE, editors. Robinson's Current Therapy in Equine Medicine. Seventh Edition, St. Louis: W.B. Saunders; 2015, p. 297–301. https://doi.org/10.1016/B978-1-4557-4555-5.00068-6.

[3] Pfister K, van Doorn D. New perspectives in equine intestinal parasitic disease: insights in monitoring helminth infections. Veterinary Clinics of North America: Equine Practice 2018;34:141–53. https://doi.org/10.1016/j.cveq.2017.11.009.

[4] Shawaf T, El-Deeb WM, Elgioushy M. The contribution of specific and nonspecific biomarkers in diagnosis of equine gastric ulcer syndrome (EGUS) under field condition. Journal of Equine Veterinary Science 2020;84:102853. https://doi.org/10.1016/j.jevs.2019.102853.

[5] Sanchez LC. Disorders of the gastrointestinal system. In: Reed SM, Bayly WM, Sellon DC, editors. Equine Internal Medicine. Fourth Edition, W.B. Saunders; 2018, p. 709–842. https://doi.org/10.1016/B978-0-323-44329-6.00012-7.

[6] Kilcoyne I, Dechant JE, Spier SJ, Spriet M, Nieto JE. Clinical findings and management of 153 horses with large colon sand accumulations. Veterinary Surgery 2017;46:860–7. https://doi.org/10.1111/vsu.12679.

[7] Dart A, Hodgson D, Snyder J. Caecal disease in equids. Australian Veterinary Journal 1997;75:552–7. https://doi.org/10.1111/j.1751-0813.1997.tb14191.x.

[8] Petersen C, Round JL. Defining dysbiosis and its influence on host immunity and disease. Cellular Microbiology 2014;16:1024–33. https://doi.org/10.1111/cmi.12308.

[9] Costa MC, Weese JS. Understanding the intestinal microbiome in health and disease. Veterinary Clinics of North America: Equine Practice 2018;34:1–12. https://doi.org/10.1016/j.cveq.2017.11.005.

[10] Dunkel B, Buonpane A, Chang Y-M. Differences in gastrointestinal lesions in different horse types. Veterinary Record 2017;181:291–291. https://doi.org/10.1136/vr.104098.

[11] Leclere M, Costa MC. Fecal microbiota in horses with asthma. Journal of Veterinary Internal Medicine 2020;34:996–1006. https://doi.org/10.1111/jvim.15748.

[12] Morrison PK, Newbold CJ, Jones E, Worgan HJ, Grove-White DH, Dugdale AH, *et al*. The equine gastrointestinal microbiome: impacts of age and obesity. Frontiers in Microbiology 2018;9. https://doi.org/10.3389/fmicb.2018.03017.

[13] Mach N, Moroldo M, Rau A, Lecardonnel J, Le Moyec L, Robert C, *et al*. Understanding the holobiont: Crosstalk between gut microbiota and mitochondria during long exercise in horse. Frontiers in Molecular Biosciences 2021;8. https://doi.org/10.3389/fmolb.2021.656204.

[14] Kauter A, Epping L, Semmler T, Antao E-M, Kannapin D, Stoeckle SD, *et al*. The gut microbiome of horses: current research on equine enteral microbiota and future perspectives. Animal Microbiome 2019;1:14. https://doi.org/10.1186/s42523-019-0013-3.

[15] Biddle A. The Equine Microbiome Project 2021. https://sites.udel.edu/equine-microbiome/equine-microbiome-project/ (accessed October 23, 2023).

[16] Costa MC, Weese JS. The equine intestinal microbiome. Animal Health Research Reviews 2012;13:121–8. https://doi.org/10.1017/S1466252312000035.

[17] Xu C, Liu J, Gao J, Wu X, Cui C, Wei H, *et al*. The effect of functional fiber on microbiota composition in different intestinal segments of obese mice. International Journal of Molecular Sciences 2021;22:6525. https://doi.org/10.3390/ijms22126525.

[18] Xiao J, Metzler-Zebeli BU, Zebeli Q. Gut function-enhancing properties and metabolic effects of dietary indigestible sugars in rodents and rabbits. Nutrients 2015;7:8348–65. https://doi.org/10.3390/nu7105397.

[19] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, *et al*. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nature Reviews Gastroenterology & Hepatology 2014;11:506–14. https://doi.org/10.1038/nrgastro.2014.66.

[20] Valcheva R, Dieleman LA. Prebiotics: Definition and protective mechanisms. Best Practice & Research Clinical Gastroenterology 2016;30:27–37. https://doi.org/10.1016/j.bpg.2016.02.008.

[21] Coverdale JA. Horse species symposium: Can the microbiome of the horse be altered to improve digestion? Journal of Animal Science 2016;94:2275–81. https://doi.org/10.2527/jas.2015-0056.

[22] O'Donnell MM, Harris HMB, Jeffery IB, Claesson MJ, Younge B, O' Toole PW, *et al.* The core faecal bacterial microbiome of Irish Thoroughbred racehorses. Letters in Applied Microbiology 2013;57:492–501. https://doi.org/10.1111/lam.12137.

[23] Van Zanten GC, Knudsen A, Röytiö H, Forssten S, Lawther M, Blennow A, *et al.* The effect of selected synbiotics on microbial composition and short-chain fatty acid production in a model system of the human colon. PLOS ONE 2012;7:e47212. https://doi.org/10.1371/journal.pone.0047212.

[24] Cooke CG, Gibb Z, Harnett JE. The safety, tolerability and efficacy of probiotic bacteria for equine use. Journal of Equine Veterinary Science 2021;99:103407. https://doi.org/10.1016/j.jevs.2021.103407.

[25] Davani-Davari D, Negahdaripour M, Karimzadeh I, Seifan M, Mohkam M, Masoumi SJ, *et al.* Prebiotics: Definition, types, sources, mechanisms, and clinical applications. Foods 2019;8:92. https://doi.org/10.3390/foods8030092.

[26] Fitzpatrick A, Roberts A, Witherly S. Larch arabinogalactan: A novel and multifunctional natural product. Agro Food Industry Hi-Tech 2004;15:30–2.

[27] Shirazi-Beechey SP. Molecular insights into dietary induced colic in the horse. Equine Veterinary Journal 2008;40:414–21. https://doi.org/10.2746/042516408X314075.

[28] Julliand V, Grimm P. Horse Species Symposium: The microbiome of the horse hindgut: history and current knowledge. Journal of Animal Science 2016;94:2262–74. https://doi.org/10.2527/jas.2015-0198.

[29] Wunderlich G, Bull M, Ross T, Rose M, Chapman B. Understanding the microbial fibre degrading communities & processes in the equine gut. Animal Microbiome 2023;5:3. https://doi.org/10.1186/s42523-022-00224-6.

[30] Weese JS. Probiotics, prebiotics, and synbiotics. Journal of Equine Veterinary Science 2002;22:357–60. https://doi.org/10.1016/S0737-0806(02)70006-3.

[31] Saastamoinen M, Fradinho M, Santos A, Miraglia N, editors. Forages and Grazing in Horse Nutrition. 2nd ed. Wageningen Academic Publishers; 2012.

[32] Ince JC, Longland AC, Moore-Colyer MJS, Harris PA. *In vitro* degradation of grass fructan by equid gastrointestinal digesta. Grass and Forage Science 2014;69:514–23. https://doi.org/10.1111/gfs.12061.

[33] Bachmann M, Glatter M, Bochnia M, Wensch-Dorendorf M, Greef JM, Breves G, *et al. In vitro* gas production from batch cultures of stomach and hindgut digesta of horses adapted to a prebiotic dose of fructooligosaccharides and inulin. J Equine Vet Sci 2020;90:103020. https://doi.org/10.1016/j.jevs.2020.103020.

[34] Ermers C, McGilchrist N, Fenner K, Wilson B, McGreevy P. The fibre requirements of horses and the consequences and causes of failure to meet them. Animals 2023;13:1414. https://doi.org/10.3390/ani13081414.

[35] Al Jassim RAM, Scott PT, Trebbin AL, Trott D, Pollitt CC. The genetic diversity of lactic acid producing bacteria in the equine gastrointestinal tract. FEMS Microbiology Letters 2005;248:75–81. https://doi.org/10.1016/j.femsle.2005.05.023.

[36] Julliand V. Impact of nutrition on the microflora of the gastro-intestinal tract in horses. Applied Equine Nutrition, vol. 1st Equine NUtrition COnference ENUCO, Hannover, Germany, 1-2 October 2005, Netherlands: Wageningen Academic Publishers; 2005, p. 85–103.

[37] Cehak A, Krägeloh T, Zuraw A, Kershaw O, Brehm R, Breves G. Does prebiotic feeding affect equine gastric health? A study on the effects of prebiotic-induced gastric butyric acid production on mucosal integrity of the equine stomach. Research in Veterinary Science 2019;124:303–9. https://doi.org/10.1016/j.rvsc.2019.04.008.

[38] Samal L, Chaturvedi VB, Saikumar G, Somvanshi R, Pattanaik AK. Prebiotic potential of Jerusalem artichoke (Helianthus tuberosus L.) in Wistar rats: effects of levels of supplementation on hindgut fermentation, intestinal morphology, blood metabolites and immune response. Journal of the Science of Food and Agriculture 2015;95:1689–96. https://doi.org/10.1002/jsfa.6873.

[39] Mourão JL, Pinheiro V, Alves A, Guedes CM, Pinto L, Saavedra MJ, *et al.* Effect of mannan oligosaccharides on the performance, intestinal morphology and cecal fermentation of fattening rabbits. Animal Feed Science and Technology 2006;126:107–20. https://doi.org/10.1016/j.anifeedsci.2005.06.009.

[40] Barker CJ, Gillett A, Polkinghorne A, Timms P. Investigation of the koala (Phascolarctos cinereus) hindgut microbiome via 16S pyrosequencing. Veterinary Microbiology 2013;167:554–64. https://doi.org/10.1016/j.vetmic.2013.08.025.

[41] French KR, Pollitt CC. Equine laminitis: loss of hemidesmosomes in hoof secondary epidermal lamellae correlates to dose in an oligofructose induction model: an ultrastructural study. Equine Veterinary Journal 2004;36:230–5. https://doi.org/10.2746/0425164044877125.

[42] Milinovich GJ, Burrell PC, Pollitt CC, Klieve AV, Blackall LL, Ouwerkerk D, *et al.* Microbial ecology of the equine hindgut during oligofructose-induced laminitis. ISME J 2008;2:1089–100. https://doi.org/10.1038/ismej.2008.67.

[43] Plancade S, Clark A, Philippe C, Helbling J-C, Moisan M-P, Esquerré D, *et al.* Unraveling the effects of the gut microbiota composition and function on horse endurance physiology. Sci Rep 2019;9:9620. https://doi.org/10.1038/s41598-019-46118-7.

[44] Berg EL, Fu CJ, Porter JH, Kerley MS. Fructooligosaccharide supplementation in the yearling horse: effects on fecal pH, microbial content, and volatile fatty acid concentrations. J Anim Sci 2005;83:1549–53. https://doi.org/10.2527/2005.8371549x.

[45] Glatter M, Borewicz K, Bogert B van den, Wensch-Dorendorf M, Bochnia M, Greef JM, *et al.* Modification of the equine gastrointestinal microbiota by Jerusalem artichoke meal supplementation. PLOS ONE 2019;14:e0220553. https://doi.org/10.1371/journal.pone.0220553.

[46] Paßlack N, Vahjen W, Zentek J. Impact of dietary cellobiose on the fecal microbiota of horses. Journal of Equine Veterinary Science 2020;91:103106. https://doi.org/10.1016/j.jevs.2020.103106.

[47] Ganda E, Chakrabarti A, Sardi MI, Tench M, Kozlowicz BK, Norton SA, *et al*. Saccharomyces cerevisiae fermentation product improves robustness of equine gut microbiome upon stress. Frontiers in Veterinary Science 2023;10. https://doi.org/10.3389/fvets.2023.1134092.

[48] Lucassen A, Finkler-Schade C, Schuberth H-J. A Saccharomyces cerevisiae Fermentation Product (Olimond BB) Alters the Early Response after Influenza Vaccination in Racehorses. Animals 2021;11:2726. https://doi.org/10.3390/ani11092726.

[49] Di Gioia D, Biavati B. Probiotics and prebiotics in animal health and Food Safety: conclusive remarks and future perspectives. In: Di Gioia D, Biavati B, editors. Probiotics and Prebiotics in Animal Health and Food Safety, Cham: Springer International Publishing; 2018, p. 269–73. https://doi.org/10.1007/978-3-319-71950-4_11.

[50] Collinet A, Grimm P, Jacotot E, Julliand V. Biomarkers for monitoring the equine large intestinal inflammatory response to stress-induced dysbiosis and probiotic supplementation. Journal of Animal Science 2022;100:skac268. https://doi.org/10.1093/jas/skac268.

[51] Sanz-Fernandez MV, Daniel J-B, Seymour DJ, Kvidera SK, Bester Z, Doelman J, *et al*. Targeting the hindgut to improve health and performance in cattle. Animals 2020;10:1817. https://doi.org/10.3390/ani10101817.

[52] Karlsson CP, Jansson A, Essén-Gustavsson B, Lindberg J-E. Effect of molassed sugar beet pulp on nutrient utilisation and metabolic parameters during exercise. Equine Veterinary Journal 2002;34:44–9. https://doi.org/10.1111/j.2042-3306.2002.tb05390.x.

[53] Siard MH, McMurry KE, Adams AA. Effects of polyphenols including curcuminoids, resveratrol, quercetin, pterostilbene, and hydroxypterostilbene on lymphocyte pro-inflammatory cytokine production of senior horses *in vitro*. Veterinary Immunology and Immunopathology 2016;173:50–9. https://doi.org/10.1016/j.vetimm.2016.04.001.

[54] Portincasa P, Bonfrate L, Vacca M, De Angelis M, Farella I, Lanza E, *et al*. Gut microbiota and short chain fatty acids: implications in glucose homeostasis. International Journal of Molecular Sciences 2022;23:1105. https://doi.org/10.3390/ijms23031105.

[55] Qin J, Li Y, Cai Z, Li S, Zhu J, Zhang F, *et al*. A metagenome-wide association study of gut microbiota in type 2 diabetes. Nature 2012;490:55–60. https://doi.org/10.1038/nature11450.

[56] Glatter M, Bochnia M, Goetz F, Gottschalk J, Koeller G, Mielenz N, *et al*. Glycaemic and insulinaemic responses of adult healthy warm-blooded mares following feeding with Jerusalem artichoke meal. Journal of Animal Physiology and Animal Nutrition 2017;101:69–78. https://doi.org/10.1111/jpn.12669.

[57] Respondek F, Myers K, Smith TL, Wagner A, Geor RJ. Dietary supplementation with short-chain fructo-oligosaccharides improves insulin sensitivity in obese horses. Journal of Animal Science 2011;89:77–83. https://doi.org/10.2527/jas.2010-3108.

[58] Heaton CP, Cavinder CA, Paz H, Rude BJ, Smith T, Memili E, *et al*. Are prebiotics beneficial for digestion in mature and senior horses? Journal of Equine Veterinary Science 2019;76:87–8. https://doi.org/10.1016/j.jevs.2019.03.116.

[59] Adams AA, Vineyard KR, Gordon ME, Reedy S, Siard MH, Horohov DW. The effect of n-3 polyunsaturated fatty acids (DHA) and prebiotic supplementation on inflammatory cytokine production and immune responses to vaccination in old horses. Journal of Equine Veterinary Science 2015;35:407–8. https://doi.org/10.1016/j.jevs.2015.03.065.

[60] Czech A, Grela ER. Influence of Bio-Mos® mannan oligosaccharides in mare diets on colostrum and milk composition and blood parameters. Engormix 2006. https://en.engormix.com/equines/horse-health/influence-bio-mos-mannan_a33830/ (accessed October 23, 2023).

[61] Vendrig JC, Coffeng LE, Fink-Gremmels J. Effects of orally administered galacto-oligosaccharides on immunological parameters in foals: a pilot study. BMC Veterinary Research 2014;10:278. https://doi.org/10.1186/s12917-014-0278-4.

[62] Vendrig JC, Coffeng LE, Fink-Gremmels J. *In vitro* evaluation of defined oligosaccharide fractions in an equine model of inflammation. BMC Veterinary Research 2013;9:147. https://doi.org/10.1186/1746-6148-9-147.

[63] Hassel DM, Curley T, Hoaglund EL. Evaluation of fecal sand clearance in horses with naturally acquired colonic sand accumulation with a product containing probiotics, prebiotics, and psyllium. Journal of Equine Veterinary Science 2020;90:102970. https://doi.org/10.1016/j.jevs.2020.102970.

[64] Niinistö K. Naturally occurring large colon sand accumulations and their medical treatment in horses. Dissertationes Scholae Doctoralis Ad Sanitatem Investigandam Universitatis Helsinkiensis. 2020.

[65] Landes AD, Hassel DM, Funk JD, Hill A. Fecal sand clearance is enhanced with a product combining probiotics, prebiotics, and psyllium in clinically normal horses. Journal of Equine Veterinary Science 2008;28:79–84. https://doi.org/10.1016/j.jevs.2008.01.004.

[66] Bachmann M, Glatter M, Bochnia M, Greef JM, Breves G, Zeyner A. Degradation of monosaccharides, disaccharides, and fructans in the stomach of Horses Adapted to a prebiotic dose of fructooligosaccharides and Inulin. Journal of Equine Veterinary Science 2021;105:103731. https://doi.org/10.1016/j.jevs.2021.103731.

[67] Sartor RB. Therapeutic manipulation of the enteric microflora in inflammatory bowel diseases: antibiotics, probiotics, and prebiotics. Gastroenterology 2004;126:1620–33. https://doi.org/10.1053/j.gastro.2004.03.024.

[68] Asadpoor M, Peeters C, Henricks PAJ, Varasteh S, Pieters RJ, Folkerts G, *et al*. Anti-pathogenic functions of non-digestible oligosaccharides *in vitro*. Nutrients 2020;12:1789. https://doi.org/10.3390/nu12061789.

[69] El-Naggar MA, Thabit TM. Evaluation of β-D-glucan biopolymer as a novel mycotoxin binder for fumonisin and deoxynivalenol in soybean feed. Foodborne Pathogens and Disease 2014;11:433–8. https://doi.org/10.1089/fpd.2013.1711.

[70] Valigura HC, Leatherwood JL, Martinez RE, Norton SA, White-Springer SH. Dietary supplementation of a Saccharomyces cerevisiae fermentation product attenuates exercise-induced stress markers in young horses. Journal of Animal Science 2021;99:skab199. https://doi.org/10.1093/jas/skab199.

[71] Spearman K. Effect of Mannan Oligosaccharie (MOS) supplementation on the immune status of mares and their foals. Master Thesis. University of Florida, 2004.

[72] Garber A, Hastie P, Murray J-A. Factors influencing equine gut microbiota: current knowledge. Journal of Equine Veterinary Science 2020;88:102943. https://doi.org/10.1016/j.jevs.2020.102943.

[73] Costa MC, Arroyo LG, Allen-Vercoe E, Stämpfli HR, Kim PT, Sturgeon A, *et al*. Comparison of the fecal microbiota of healthy horses and horses with colitis by high throughput sequencing of the V3-V5 region of the 16s rRNA gene. PLOS ONE 2012;7:e41484. https://doi.org/10.1371/journal.pone.0041484.

[74] Wemer H, Bames L. Effects of administration of an oral arabinogalactan supplement on mares and foals. Equine Nutrition and Physiology Society (ENPS) Symposium Proceedings.

[75] Jin Song S, Woodhams DC, Martino C, Allaband C, Mu A, Javorschi-Miller-Montgomery S, *et al*. Engineering the microbiome for animal health and conservation. Experimental Biology in Medicine 2019;244:494–504. https://doi.org/10.1177/1535370219830075.

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