Demonstrated Prebiotic Applications

Emerging Challenges in the Production Animal Industry

Natural events, government regulations, and changing consumer values all influence the production animal industry. In the case of the North American swine industry, these factors converged almost simultaneously. Porcine Epidemic Diarrhea virus (PEDv), which infects the intestinal tissue and causes severe dehydration and death in piglets, was first detected in April 2013 in the United States[1] before spreading to Canada in 2014[2]. PEDv continues to have an impact on the swine industry today, with the recent outbreak in Canada in 2019[3]. Piglets infected with PEDv display an altered microbiome with increased pathogenic bacteria and most die within a week of infection[4]. In one year, PEDv was responsible for the loss of approximately 7 million pigs in the United States[5].

Canadian rules regulating the subtherapeutic use of Medically Important Antimicrobials in piglets changed in 2018, preventing Own Use Importation of these products by producers[6]. These changes were due in part to growing public concerns over antimicrobial resistance and the presence of antibiotics in the food chain. The full impact of restricted antibiotic usage during the Canadian PEDv crisis remains to be determined but this scenario highlights the importance of digestive health in livestock production and the need for alternatives to antibiotics.

Alternatives to Antibiotics

Preventing diarrhea in production animals remains a difficult challenge due to housing requirements and standard facility operations. Research on the gut microbiome has identified imbalances in this ecosystem as a major cause of diarrhea. In searching for alternatives to antibiotics, microbiome therapeutics that mimic antibiotics via temperature-stable, in-feed application are most compatible with existing infrastructure and therefore most appealing. Probiotic supplementation involves the introduction of a novel or under-represented living microbe (or microbes) with the aim of influencing the ecosystem to inhibit diarrhea. Unfortunately, the storage of high quality probiotics typically requires low temperatures and most efforts to introduce microbes into the ecosystem have limited success[7].

Postbiotics, which include components of the bacterial cell or metabolic breakdown products, aim to influence physiology by mimicking certain activities of the microbiome[8]. Short chain fatty acids (SCFAs) are well-characterized postbiotics[9] but delivery to the site of activity (typically the colonic epithelium and systemic circulation) requires formulations or technical modifications that limit applicability[10]. Furthermore, we have limited understanding of how postbiotics affect our physiology and the effectiveness of postbiotics delivered outside of the context of the microbiome remains to be determined.

Prebiotics are fermentable substances that resist digestion, becoming 'food' for the gut microbiome. Rather than colonizing the microbiome with specific probiotics, prebiotic supplementation stimulates the growth and activity of endogenous probiotics[11]. This facilitates the delivery of postbiotic molecules like SCFAs directly to the lumen of the colon where they are physiologically active. Furthermore, the indigestible, inert nature of prebiotics means that they can be consumed as an in-feed additive.

MSP[RS] is a prebiotic digestion resistant starch (DRS) derived entirely from Solanum tuberosum tuber. This insoluble prebiotic contains large amylose and amylopectin molecules with high degrees of polymerization. The prebiotic effects of MSP[RS] have been evaluated in swine. This patented technology (US9861654B2; WO2014036655A1) is consumed by millions of weanling pigs annually, helping to reduce antibiotic usage and stop scours.

The treatment of diarrhea using MSP[RS] was studied in collaboration with Dr. Martin Nyachoti at the University of Manitoba. In the first study, dietary supplementation with MSP[RS] at 7% was shown to be as effective as antibiotic treatment (0.01% of diet; Aureo SP250: Chlortetracycline, Penicillin, Sulfamethazine) in preventing diarrhea (Fig 1)[12]. In the second study, very low inclusion rates of 0.5 - 1.0% were found to have improved fecal consistency (Fig 2)[13].

Figure 1

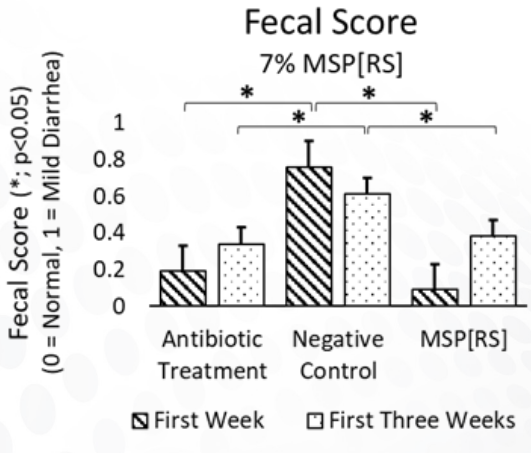
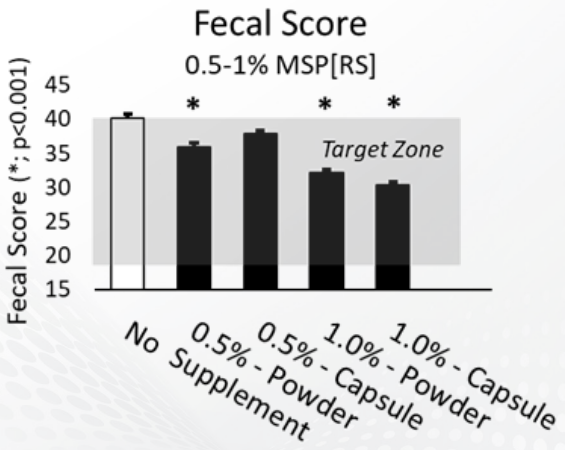


Figure 2



Furthermore, very low inclusion rates of MSP[RS] had a positive influence on the pH and abundances of the gut microbiome fermentation end products known as volatile fatty acids (VFAs), including branched chain fatty acids (BCFAs), which are the byproduct of protein fermentation[14].

Table 1. Cecal pH and VFA concentrations (mM) in weaned pigs fed a basal diet with MSP[RS] or without for 28 d after weaning. [a,b]Means within a row with different superscript letter significantly differ ($p < 0.05$).

Variable	No Supplement	0.5% Powder	0.5% Capsule	1.0% Powder	1.0% Capsule	Pooled SEM	*p* value
pH	6.4[a]	6.2[b]	6.3[b]	6.2[b]	6.2[b]	0.0	< 0.001
Acetate	42.9[a]	54.0[b]	50.8[b]	53.8[b]	53.2[b]	0.5	<0.001
Propionate	19.5[b]	21.9[ab]	24.1[a]	21.4[ab]	21.4[ab]	0.5	0.083
Isobutyrate	0.14	0.14	0.11	0.12	0.09	0.01	0.679
Butyrate	11.3	12.2	12.3	14.7	13.4	0.4	0.118
Isovaleric acid	0.41	0.32	0.28	0.32	0.26	0.03	0.420
Valeric acid	3.0	2.0	2.1	1.5	1.9	0.2	0.208
Total VFA	77.3[a]	90.5[b]	89.7[b]	91.9[b]	90.3[b]	0.8	<0.001
BCFAs, %	4.7[a]	2.6[b]	2.8[b]	2.1[b]	2.6[b]	0.3	0.029

Together, these findings demonstrate that MSP[RS] stimulates a healthy digestive tract through microbial fermentation that generates beneficial volatile fatty acids and lowers pH, which together reduce diarrhea and help promote normal fecal consistency.

MSP[RS]® Prebiotic Differentiation Points:

- Validated proprietary production process .
- Temperature-stable, suitable for in-feed applications .
- Well-tolerated, flavorless, single ingredient prebiotic derived from a natural source.
- Insoluble nature creates no osmotic effects or discomfort in the small intestine.
- Large molecular structure facilitates very slow fermentation, avoiding rapid gas accumulation and associated discomfort.
- The Company is vertically integrated with a state of the art manufacturing and packaging facility in Manitoba, Canada with a site license from Health Canada.

msp[RS]® RESISTANT STARCH

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