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Extension and Outreach

Feed Additives to Mitigate the Risk of Virus-contaminated Feed

The introduction of Porcine Epidemic Diarrhea Virus (PEDV) in 2013 into the US swine industry pointed toward feed ingredients as the likely route of introduction[1]. Subsequent research trials have documented viruses can survive in feed ingredients and complete feed for transoceanic shipping[2] (30 and 37 days) and transcontinental shipping[3] (23 days.) Authors of the transoceanic trial concluded: 1. Viruses can survive in feed, but survival is variable and depends on specific properties of each virus; 2. Certain feed ingredients or feed products present a better matrix for virus survival than others; and 3. Select ingredient matrices seemed to enhance the survival of multiple viruses.

This fact sheet focuses on three research papers which evaluated compounds to mitigate virus-contaminated feed. The compounds are classified into two different groups. Foreign Animal Disease (FAD) viruses: African Swine Fever (ASF) and Foot and Mouth Disease (FMD); and Domestic viruses: Porcine Reproductive and Respiratory Syndrome virus (PRRSV), Senecavirus A (SVA), and Porcine Epidemic Diarrhea virus (PEDV) are discussed.

African Swine Fever Virus (ASFV) Trial[4]

ASFV is transmissible through natural consumption of contaminated swine feed and is broadly stable across a wide range of feed ingredients commonly imported into the US. Medium-chain fatty acid (MCFA) and formaldehyde-based feed additives were tested in cell culture and in feed ingredients under a transoceanic shipment model (30 days with varying temperature and humidity.)

The formaldehyde source was composed of 37% aqueous formaldehyde and propionic acid (Sal CURB®, Kemin Industries, Inc.) with 0.33% inclusion rate; the MCFA source (MCFA, Sigma-Aldrich) was a blend including an equal volume ratio (1:1:1) of hexanoic acid (C6), octanoic acid (C8), and decanoic acid (C10) with a 1% inclusion rate.

Feed or ingredients included conventional soybean meal, organic soybean meal, soy oil cake, choline, moist dog food, moist cat food, dry dog food, pork sausage casings, and complete feed in meal form. Feed additives were incorporated into feed or ingredients at day 0 and challenged with ASFV (Georgia 2007) on day 0. All samples collected on day 30 with detectable ASFV DNA on qPCR, but negative for infectious virus on PAMs tested in a pig bioassay. High health pigs (24 days old) were acclimated for three days, then received one or two 1-ml injections in the hind limbs for testing up to two

different feed sample types. Pigs were monitored for clinical signs of ASF, including fever, lethargy or depression, dyspnea, or tachypnea. Both chemical additives reduced ASFV infectivity in a dose-dependent manner. This study provides evidence that chemical feed additives may potentially serve as mitigants for reducing the risk of ASFV introduction and transmission through feed.

Authors noted: In this study, the presence of detectable ASFV DNA by qPCR was found in all samples treated with MCFA or formaldehyde, despite those samples being primarily negative for infectious virus based on virus isolation and pig bioassay. This is important as inactivation criteria for feed additive efficacy against ASFV should not be reliant on a lack of DNA detection on PCR. Due to nucleic acid stability and detection throughout the 30 days in all samples, qPCR would be an appropriate tool for diagnostic screening of feed samples at high risk for ASFV contamination, with confirmatory testing of positive samples on virus isolation.

Foot and Mouth Disease Virus (FMDV) Trial[5]

The ability of FMDV (virus strain A24) to cause infection in exposed pigs was mitigated by pre-treatment of feed with two commercially available feed additives, based on either formaldehyde (Sal CURB®) or lactic acid (Guardian™).

In this trial, feed mitigants were added to feed 24 hours prior to FMDV contamination, and the contaminated feed was allowed another 24-hour incubation at room temperature prior to feeding to the pigs. Sal CURB®, a formaldehyde-based feed additive, with inclusion rate of 0.33% (by weight), effectively reduced the infectivity of FMDV. None of the pigs consuming Sal CURB®-treated feed became infected, compared to three out of four pigs that were infected by two days post exposure (dpe) in the positive control group (no feed additive.) Guardian, a lactic acid-based feed additive, with inclusion rate of 0.44% (by weight) reduces FMDV infectivity in feed, despite questionable reduction in viral viability in the in vitro study. Authors noted Guardian is added to the feed in powder form, which may account for the differences observed in vitro versus in vivo as the overall acidifying effect may be enhanced by salivation and deglutination during eating. While none of the pigs in the Guardian group had clinical signs of FMD, one of four pigs had three consecutive oropharyngeal (OP) swab samples that were positive for FMDV RNA (2, 4, and 6 dpe) as well as detectable neutralizing anti-FMDV antibodies at 14 dpe, suggesting a subclinical infection that did not transmit within the group.

Medium-chain fatty acid (MCFA) additives have proven antiviral activity against enveloped viruses[6,7], but there is little evidence for their efficacy against non-enveloped viruses like FMDV. Authors noted CaptiSURE™ had little to no anti-FMDV activity in vitro, and therefore was not evaluated in vivo.

Domestic Virus Trial (PRRSV, PEDV, SVA)[8]

The objective of this study was to evaluate the ability of feed additives to mitigate the risk of virus-contaminated feed using a model based on real-world conditions. Equal concentrations of porcine reproductive and respiratory syndrome virus (PRRSV), Senecavirus A (SVA), and porcine epidemic diarrhea virus (PEDV) were used to challenge pigs. The study evaluated 15 additives across five independent experiments, in facilities that housed 96 pigs per rooms for each treatment. Each room had separate ventilation systems (air filtered in and out), manure pits, dedicated feed bins, and Danish entry system with room-specific coveralls, boots, and gloves.

Separate batches of feed were manufactured for each feed additive for the 25-day feeding period. Each experiment used a 10-day pre-challenge period to acclimate pigs to their surroundings and respective diets, followed by a 15-day post-challenge period to measure response. Feed contamination (challenge) occurred on days 0 and 6 using a 500 ml block of ice (containing equal concentration of PRRSV-174, PEDV, and SVA), which was manually dropped into the bin through its opening at the top. Feed then was delivered as needed into each animal room via the auger system and consumed by natural feeding behavior.

After challenge, samples were collected on day 6 and day 15 at the pen level (feed troughs and oral fluids) and at the animal level (clinical signs, viral infection, growth rate, and mortality) across five independent experiments involving 15 additives. On day 15 post-challenge, the experiment was terminated, final samples collected, and all animals humanely euthanized via captive bolt. Thirty of the 96 animals from each room were selected for necropsy.

Data results revealed that all three viruses consistently entered the treatment and control rooms via the feed, and that viral RNA was subsequently detected in the oral cavities of pigs, indicating that the pigs were exposed to the viruses via the feed. With limited sampling periods, the time between challenge and detection seemed to vary across the five experiments.

Authors reported: "Under the conditions of this study, it appeared that the majority (14 of 15; Vigilex was the exception) of products significantly improved pig health and performance as compared to pigs raised on non-mitigated diets. Treatment of contaminated feed with 10 out of 15 products (Activate DA at 0.5%, Sal CURB®, CaptiSURE™ at 1.0% and 0.5%, R2™, Guardian, DaaFit® PLUS, pHorce, VVC at 0.5% and 0.3%, Dual Defender™, and Furst Protect) led to no signs of clinical disease and a mortality level of ≤1%."

Three products (Sal CURB®, CaptiSURE™ at 1.0% and 0.5, and VVC at 0.5% and 0.3%) had no clinical signs and have 0 or 1 PCR positive samples out of 30 (1 out of 30 could be false positive) for rectal swabs, and serum and0 tonsil testing.

Authors acknowledged: "These results raise questions regarding the mechanism of action. It is possible that the products are ameliorating the disease at the level of the virus through a reduction in viral load or viability, or at the level of the pig through enhancement of the immune system, adjustment to the gut environment, manipulation of the microbiome, or by some other mode. As this observation was consistent across a diverse portfolio of products, that is monovalent and multivalent organic acid products; short-, medium-, and long-chain fatty acid blends; monoglycerides of fatty acids; formaldehyde-

Table 1. Summary of feed additives tested and observed results from Domestic Virus Trial (equal challenge of PRRS, SVA, PEDV).

Product	Company	Description	Study Inclusion rate(s)	No evidence of infection via PCR in rectal, tonsil and serum samples	No signs of clinical disease and mortality level of <1%
Activate DA	Novus	A blend of organic acids and methionine hydroxy analogue (HMTB[a])	0.5% or 0.15%		X (at 0.5%)
Sal CURB®	Kemin	A blend of aqueous formaldehyde and organic acids	0.275%	X (at 0.275%)	X (at 0.275%)
Sal CURB® K2	Kemin	An organic acid blend, including formic acid, ammonium formate, propionic acid, and lactic acid	0.275%		
CaptiSURE™	Kemin	Medium-chain fatty acid blend	0.5% or 1.0%	X (at 0.5% and 1.0%)	X (at 0.5% and 1.0%)
Daafit® S	ADM	A source of fatty acids, including lauric and myristic acids and glycerol mono laurate	0.5% or 0.3%		
Daafit® Plus	ADM	Acidifier blend composed of short-chain fatty acids, formic, propionic acid, acetic acid, sorbic acids, and a blend of medium-chain fatty acids including lauric acid, caprylic acid, and glycerol-mono-laurate	0.5%		X (at 0.5%)
Dominnate	Purina Animal Nutrition	A blend of 3 medium-chain fatty acids	0.5%		
Finio®	Anitox	A blend of propionic acid, trans-2-hexenal (leaf aldehyde), and nonanoic acid (pelargronic acid)	0.2%		
Guardian	Alltech	A blend of organic acids and essential oils	0.44%		X (at 0.44%)
R2™	Feed Energy	A natural lipid-based line of products made by a combination of short-, medium-, and long-chain fatty acids	3.0%		X (at 3.0%)
VVC	DSM	Pure benzoic acids with nature-identical flavorings	0.5% or 0.3%	X (at 0.3% and 0.5%)	X (at 0.3% and 0.5%)
Vigilex	Provimi	A blend of oils, bacterial fermentation products, whey products, plant protein, and natural flavorings	0.4%		
pHorce	Anpario	A blend of liquid formic and propionic acids on a mineral carrier	0.3%		X (at 0.3%)
Dual Defender™	Ralco	A blend of essential oils and prebiotic fiber	0.1%		X (at 0.1%)
Furst Protect	McNess	A blend of emulsifying monoglycerides of medium-chain fatty acids and essential oils, plus botanical extracts	0.4%		X (at 0.4%)

based products; and essential oils (Table 1), there appears to be great opportunity for future research in this area."

Feed additives being marketed (as of November 2021)

Since the completion of the Domestic Virus Trial8 some feed additives have been discontinued and new products are being tested and marketed. An updated list of available products has been compiled by Kansas State University Research and Extension. The "Summary of feed additives with scientific evidence evaluating efficacy against viral pathogens in swine feed" (asi.k-state.edu/research-and-extension/feedsafetyresources/KSUFeedAdditiveSummary%20-%20November%202021.pdf) document includes current product offerings, suggested inclusion rate per ton, relative cost per ton, and company contact information. Check for document updates at www.ksufeed.org.

The intent is to provide awareness of product formulation and pricing and encourage reaching out to the company for more specific applications and pricing for your operation.

We must acknowledge claims of efficacy for reduction of viral contamination have not been reviewed or approved by the United States Food and Drug Administration for many of the products described in this document. Therefore, within this document there are no claims directed (whether stated or implied) beyond what is provided on the manufacturer label.

Disclaimer: Information is provided for awareness of products and formulations and is not a statement of endorsement for companies or products presented, nor is criticism implied for companies or products not listed.

Considerations

This is exciting research to identify tools that may help reduce or address specific viruses in swine production. Each operation will need to evaluate the cost/benefit to incorporate these products into their feeding program. While the focus of this paper was to mitigate the risk of virus-contaminated feed, some additives may reduce bacterial population, lower gut pH, or bring additional benefits.

The greatest potential for benefit for most operations will be in the sow herd, then nursery, and then finishing. While continuous use of these products may be justified, other situations may benefit from using a "flush" (example: one week a month) or seasonally (example: November to January during higher PRRS pressure). The authors acknowledge these are concepts that merit further research.

The diversity of product formulations and potential modes of action will foster additional research and further understanding.

Authors

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Resources

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